NICKEL PEROXIDE OXIDATION OF ORGANIC COMPOUNDS

A Thesis Submitted
In Partial Fulfilment of the Requirements
for the Degree of
DOCTOR OF PHILOSOPHY

BY
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D E D I C A T E D T O

M Y

T E A C H E R S

CONTENTS

STATEMENT

I hereby declare that the matter embodied in this thesis is the result of investigations carried out by me in the Department of Chemistry, Indian Institute of Technology, Kanpur, India, under the supervision of Professor M.V. George.

In keeping with the general practice of reporting scientific observations, due acknowledgement has been made wherever the work described is based on the findings of other investigators.

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CERTIFICATE I

This is to certify that Mr. K.S. Balachandran has satisfactorily completed all the courses required for the Ph.D. degree programme. These courses include:

Chm 500	Mathematics for Chemists I
Chm 501	Advanced Organic Chemistry I
Chm 502	Advanced Organic Chemistry II
Chm 521	Chemical Binding
Chm 523	Chemical Thermodynamics
Chm 524	Modern Physical Methods in Chemistry
Chm 541	Advanced Inorganic Chemistry I
Chm 602	Chemistry of Natural Products
Chm 613	Chemistry of Macromolecules
Chm 622	Chemical Kinetics
Chm 800	General Seminar
Chm 801	Special Graduate Seminars
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CERTIFICATE II

Certified that the work contained in this thesis entitled: "Nickel Peroxide Oxidation of Organic Compounds" has been carried out by Mr. K.S. Balachandran under my supervision and the same has not been submitted elsewhere for a degree.

M.V. George

M.V. George
Thesis Supervisor

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K.S. Balachandran

PREFACE

Numerous metal oxides such as nickel peroxide, manganese dioxide, mercuric oxide, lead peroxide and silver oxide have been extensively used in the oxidation of a wide variety of organic compounds. The thesis entitled: "Nickel Peroxide Oxidation of Organic Compounds" deals with the oxidation of different organic compounds employing nickel peroxide in non-aqueous medium. The thesis is divided into five chapters.

Chapter I deals with a comparative general survey of the literature on the oxidation of different organic substrates, employing both nickel peroxide and manganese dioxide.

In Chapter II, the results of our studies concerning the oxidation of benzylideneacetone phenylhydrazones with nickel peroxide are discussed. It has been shown that benzylideneacetone phenylhydrazone on oxidation gives an oxidative dimer which has been identified as dl-1,1',5,5'-tetraphenyl-3,3'-dimethyl-4,4'-bipyrazoline. Under similar conditions, 3-methylbenzylideneacetone phenylhydrazone gives a mixture of dl- and meso-1,1'-diphenyl-3,3'-dimethyl-5,5'-di(m-tolyl)-4,4'-bipyrazolines. Similarly, product mixtures consisting of dl- and meso-4,4'-bipyrazolines have been obtained from 3-chloro- and 4-chlorobenzylideneacetone phenylhydrazones and piperonylideneacetone phenylhydrazone. On the other hand, the oxidation of 2-methyl-, 4-methyl- and 2-chlorobenzylideneacetone phenylhydrazones and furfurylideneacetone phenylhydrazone gives the

corresponding meso-4,4'-bipyrazolines only. Some preliminary studies concerning the mass spectral fragmentation of a few 4,4'-bipyrazolines have also been carried out.

Chapter III deals with the oxidation of 1,2-diketone bisphenylhydrazones. It has been observed that different products are formed in these reactions, depending on the nature of the starting materials and the reaction conditions. Glyoxal bisphenylhydrazone, methylglyoxal bisphenylhydrazone, biacetyl bisphenylhydrazone, acenaphthenequinone bisphenylhydrazone, benzil bisphenylhydrazone, 4,4'-dimethoxybenzil bisphenylhydrazone and 4,4'-dichlorobenzil bisphenylhydrazone on oxidation with nickel peroxide, at room temperature, give the corresponding bisphenylazoolefins. In addition, 1,2,3-triazoles are obtained in the oxidation of benzil and 4,4'-dimethoxybenzil bisphenylhydrazones. Phenylmethylglyoxal bisphenylhydrazone, on oxidation, gives 1,3-diphenyl-4-phenylazopyrazole, both at room temperature and under refluxing conditions. Similarly, 4-phenylazopyrazoles are obtained in the oxidation of methylglyoxal bisphenylhydrazone and biacetylbisphenylhydrazone under refluxing conditions in benzene.

In the case of the oxidation of benzylmethylglyoxal bisphenylhydrazone, in addition to 1,5-diphenyl-3-methyl-4-phenylazopyrazole, both 4-phenyl-3-phenylazo-3-buten-2-one phenylhydrazone and 1-phenyl-3-benzoyl-4-phenylazopyrazole are also isolated. The oxidation of phenylglyoxal bisphenylhydrazone, on the other hand, gives a mixture of 2,5-diphenyl-1,2,3-triazole and 2,3,5,6-tetraphenyl-1,2,4,5-tetraazapentalene.

The oxidation of benzoylhydrazones of aldehydes, ketones and 1,2-diketones have been reported in Chapter IV. Aldehyde benzoylhydrazones, for example, undergo oxidative cyclization giving rise to 1,3,4-oxadiazole derivatives. In addition, 2:1-nickel complexes could also be isolated from these reactions. Under similar conditions, ketone benzoylhydrazones give rise to the corresponding ketones and Schiff's bases. Biacetyl bisbenzoylhydrazone on oxidation with nickel peroxide gives 1-α-benzoyloxybenzylideneamino-4,5-dimethyl-1,2,3-triazole and nickel-biacetyl bisbenzoylhydrazone. Similarly, benzil bisbenzoylhydrazone gives the corresponding 1,2,3-triazole and the nickel complex. In contrast, phenylglyoxal and 4-methoxyphenylglyoxal bisbenzoylhydrazones give in each case a mixture of 1-dibenzoylamino-4-substituted-1,2,3-triazole, 1-benzoylamino-4-substituted-1,2,3-triazole and a 2:1 nickel complex. Phenylmethylglyoxal bisbenzoylhydrazone, on the contrary, gives only the corresponding enol-benzoate.

Chapter V deals with the oxidation of several organic compounds with nickel peroxide. Benzylidene-o-phenylenediamine and 2-nitro-, 3-nitro- and 4-nitrobenzylidene-o-phenylenediamines on oxidation give the corresponding benzimidazoles. The oxidation of 2-hydrazinobenzothiazole with nickel peroxide gives different products depending on the nature of the solvents used. Thus, in benzene it gives benzothiazole, 2-phenylbenzothiazole and biphenyl, whereas, in toluene, benzothiazole, bis-2,2'-benzothiazolyl and benzaldehyde are isolated. In

contrast, when chloroform is used, both benzothiazole and 2,2'-azodibenzothiazolyl are isolated. The oxidation of N-aminophthalimide with nickel peroxide results in the formation of phthalimide, assumed to be formed through a tetrazene intermediate. The oxidation of N-(2-aminophenyl)-pyrrolidine, on the other hand, gives the oxidative cyclization product, 1,2-trimethylenebenzimidazole, along with small amounts of 2,2'-di-(N-pyrrolidinyl)-azobenzene.

CHAPTER I

OXIDATIONS EMPLOYING NICKEL PEROXIDE AND MANGANESE DIOXIDE A COMPARATIVE STUDY

I.1 INTRODUCTION

Numerous examples of the oxidation of organic compounds using metal oxides such as nickel peroxide[1] and manganese dioxide[2] are reported in the literature. Manganese dioxide and nickel peroxide show similar behaviour in most of the oxidation reactions, although nickel peroxide appears to be a more powerful oxidizing agent. In general, the yields of the products formed in nickel peroxide oxidations are better as compared to the manganese dioxide oxidations. However, there are several examples of reactions wherein these two oxidizing agents give rise to different products. The present discussion primarily deals with the oxidation of different substrates, where both manganese dioxide and nickel peroxide have been used. Both these oxides serve as selective reagents for the oxidation of different functional groups.

I.2 OXIDATION WITH NICKEL PEROXIDE

The use of nickel peroxide in oxidizing organic compounds was first reported in a German patent[3], in which

the oxidation of toluene to benzaldehyde and benzoic acid was described. Weijlard[4] reported that diacetone-2-ketone-L-gulonic acid, an intermediate in the synthesis of vitamin C was obtained from diacetone-L-sorbose in good yields by the addition of nickel salts in a solution of sodium hypochlorite. Nakagawa[5] had suggested that the black oxide of nickel formed by the treatment of sodium hypochlorite with nickel sulfate was responsible for this type of oxidation. Since then several workers have used this reagent for oxidizing different organic substrates.[1]

The oxidation of organic compounds using nickel peroxide is assumed to proceed through a free-radical pathway.[1,6-9] Isotopic and esr studies using radical scavengers support this view.[6-9] Nickel peroxide has a large surface area as compared to its weight and hence it serves as a better oxidizing agent as compared to manganese dioxide. In addition, only smaller quantities of the reagent (1.0 - 1.5 equivalents) are needed for oxidation, when compared to similar reactions employing manganese dioxide.

I.3 ALCOHOLS

The oxidation of alcohols by nickel peroxide is affected by the alkalinity of the solvent medium and also the reaction temperature.[10] While the oxidation of alcohols in organic solvents like benzene and petroleum ether affords the corresponding carbonyl compounds, primary alcohols in aqueous alkaline solutions are further oxidized to the corresponding carboxylic acids. Manganese dioxide, on the other hand,

oxidizes alcohols to the corresponding carbonyl compounds only.

I.3.1 Oxidation in Aqueous Alkaline Medium

Saturated aliphatic primary alcohols are readily converted to the corresponding carboxylic acids on treatment with nickel peroxide, in alkaline medium.[10] In general, the oxidation of straight chain alcohols proceeds, more rapidly than that of the corresponding branched chain isomers. Unsaturated alcohols, on the other hand, undergo oxidative cleavage in some cases. Allyl alcohol, for example, on treatment with nickel peroxide is partially cleaved to give both formic acid and carbon dioxide, along with acrylic acid, the major oxidation product.[10] The oxidation of propargyl alcohol, however, gives mainly propiolic acid. Similarly, cinnamyl alcohol undergoes smooth conversion to cinnamic acid.

In the case of alcohols possessing an active methylene group, the methylene group is in part, simultaneously oxidized at room temperature to give compounds with less number of carbon atoms. However, at lower temperatures, the hydroxylic function alone is affected. Thus, the oxidation of β-phenylpropyl alcohol at 0° gives mainly β-phenylpropionic acid along with traces of benzoic acid, whereas, at 30° a much higher yield of benzoic acid is obtained.[10]

Nickel peroxide has been used for the synthesis of orotic acid and thioorotic acid derivatives.[11] Thus, the oxidation of 6-hydroxymethyl-1-methyluracil (1) with nickel peroxide is reported to give 1-methylorotic acid (2).

Similarly, 6-hydroxymethyl-1-methylthiouracil (3) gives 1-methyl-2-thioorotic acid (4). With excess of nickel peroxide, however, 1-methylorotic acid (2) is formed from 3 (Scheme I.1).

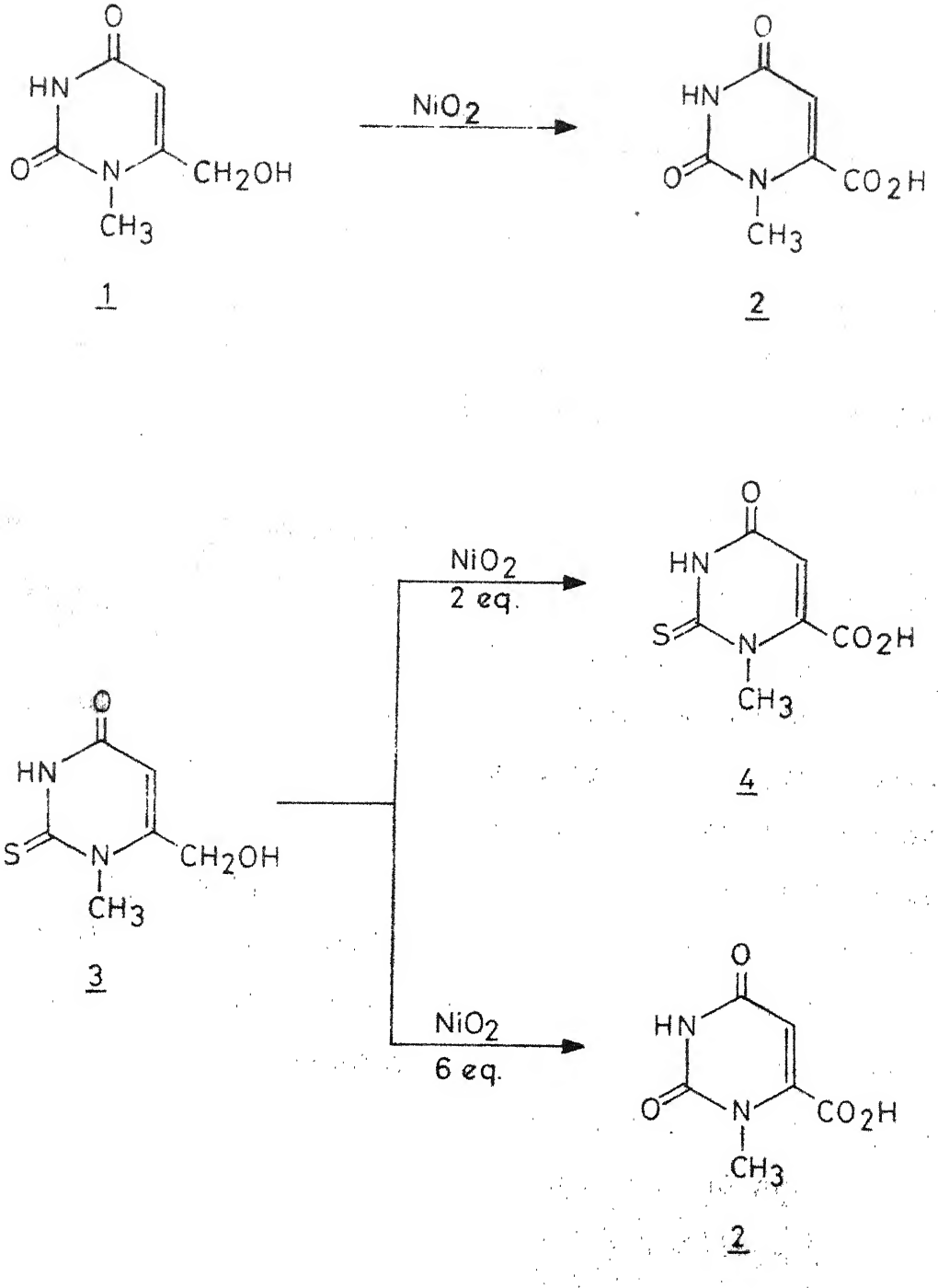
Benzylic alcohols are easily oxidized to the corresponding carboxylic acids on treatment with nickel peroxide. Thus, benzyl alcohol and o-methylbenzyl alcohol give benzoic acid and o-toluic acid, respectively.[10] Oxidation of m-methylbenzyl alcohol and p-methylbenzyl alcohol at low temperatures, gives m-toluic and p-toluic acid, respectively. At higher temperatures, however, both metaphthalic acid and terephthalic acid, respectively, are formed, along with the corresponding monocarboxylic acids.[10]

The oxidation of α-furfuryl alcohol with acidic oxidizing agents results in ring opening reactions but with nickel peroxide, pure α-furoic acid is readily obtained.[10]

I.3.2 Oxidation in Organic Solvents

Alcohols are readily converted to the corresponding carbonyl derivatives, when treated with nickel peroxide in organic solvents such as benzene or petroleum ether.[10] The oxidation of saturated aliphatic alcohols with nickel peroxide, employing equivalent amounts of the oxide and alcohol give poor yields of the carbonyl compounds and most of the available oxygen in the oxidizing agent gets lost as oxygen.[10] In contrast, manganese dioxide oxidizes saturated aliphatic primary and secondary alcohols to the corresponding carbonyl compounds in good yields.[12,13]

Scheme 1·1



It is interesting to note that in the oxidation of alcohols with nickel peroxide using chloroform as solvent, no carbonyl compounds are formed, but hexachloroethane has been isolated in appreciable amounts.[10] It is apparent that chloroform is undergoing an oxidative dimerization in presence of nickel peroxide.

Benzylic alcohols and their α-substituted analogues have been oxidized both by nickel peroxide[10] and manganese dioxide[14-25] to give the corresponding carbonyl derivatives. Thus, benzyl alcohol[10] and benzhydrol[15] are oxidized to benzaldehyde and benzophenone, respectively, in each case. It has been found that compared to the manganese dioxide oxidation of benzyl alcohol, nickel peroxide gives better yields of benzaldehyde with lesser amounts of the oxidizing agent. Because of their mild and selective nature, both the oxidizing agents have been used in the oxidation of heterocyclic alcohols like furfuryl alcohol to give the corresponding aldehydes.[10,26]

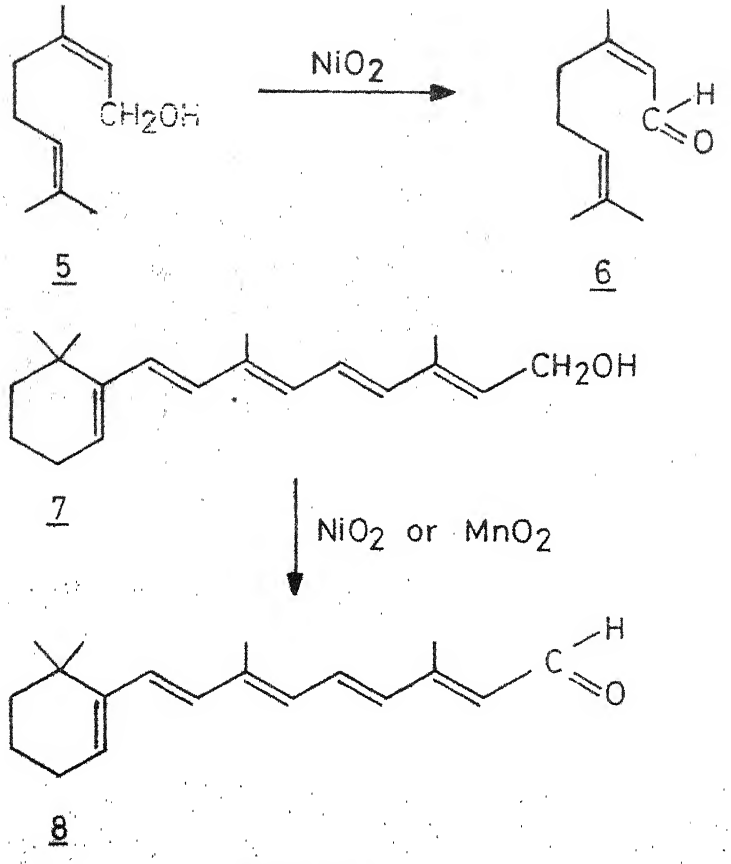
Manganese dioxide is an excellent reagent for the oxidation of allylic alcohols. The simplest α,β-unsaturated alcohol, allyl alcohol,[27,28] is oxidized to acrolein while cinnamyl alcohol[28] is oxidized to cinnamaldehyde. Similarly, nickel peroxide also oxidizes allylic alcohols to the corresponding unsaturated aldehydes. It has been reported that the oxidation of geraniol (5) with manganese dioxide results in a low yield of citral (6) even after more than 90 hr.[28] However, in the case of nickel peroxide oxidation, citral (6)

is formed in a 81% yield in 6 hr.[10] Similarly, the oxidation of vitamin A (7) with nickel peroxide[10] gives a 83% yield of retinene (8) in 1 hr as compared to the manganese dioxide oxidation[29] which requires 18 hr (Scheme I.2). The mechanism of the nickel peroxide oxidation of alcohols has been studied in detail using O^{18}-labelled substrates. It has been observed that the initial reaction involves the abstraction of a proton from the α-position of alcohols followed by hydrogen abstraction from the hydroxy group to give the appropriate carbonyl compounds.[6]

I.4 PHENOLS

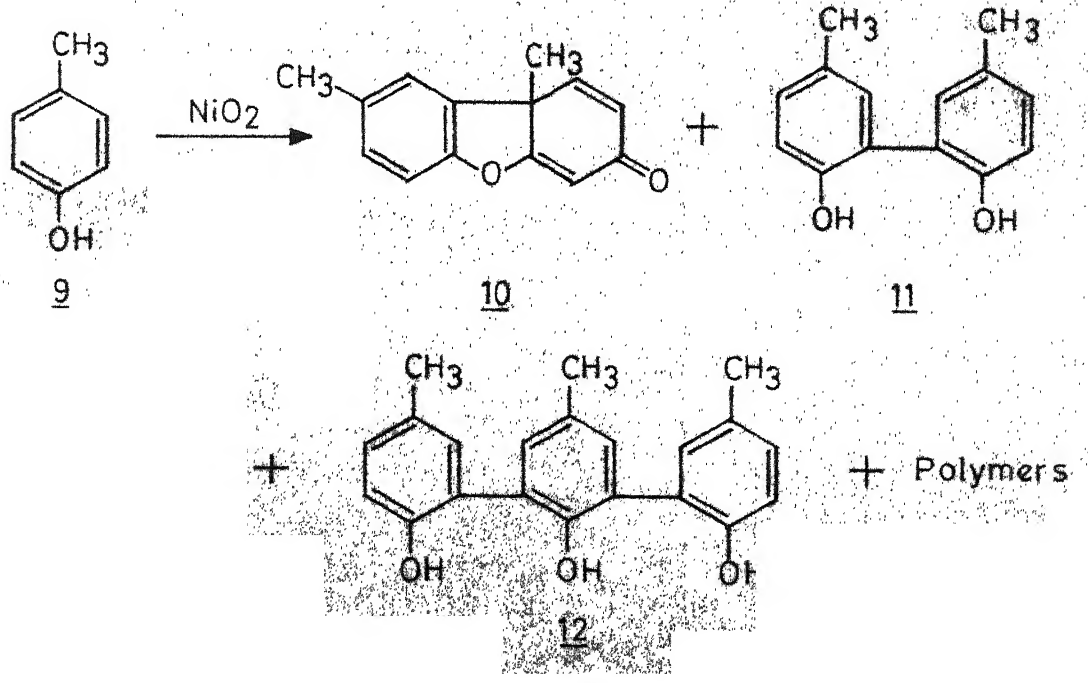
Numerous reports have appeared on the oxidation of both natural and synthetic phenolic antioxidants employing a variety of oxidizing agents.[30,31] The products formed in these oxidations depend considerably on the nature of the oxidizing agents and the reaction conditions. Phenol is reported to undergo oxidation in presence of nickel peroxide to give polymeric materials. However, a compound such as p-cresol (9), on treatment with nickel peroxide in benzene solution or in aqueous alkaline medium gives rise to a mixture of compounds consisting of the ketone 10, the ortho-isomer 11 and a trimer 12, in addition to polymeric materials (Scheme I.3).[32] The oxidation of 2,6-xylenol (13) in benzene gives rise to poly-2,6-dimethylphenylene ether (14) and a small amount of 3,3',5,5'-tetramethyl-4,4'-diphenoquinone (15). However, only the polymeric material 14 is isolated, if the oxidation is carried out in aqueous sodium hydroxide solution (Scheme I.3).[32] In

Scheme I·2



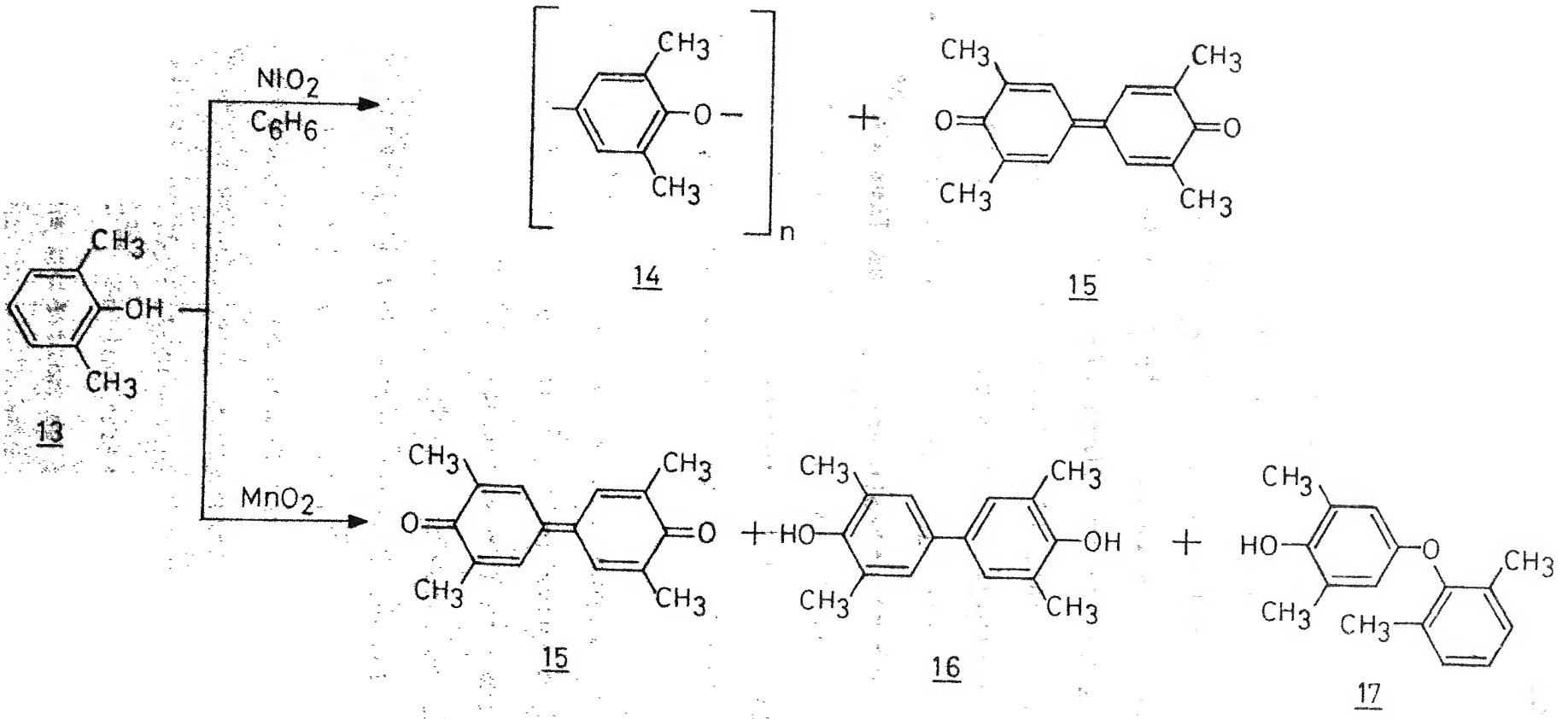
5 6 7 8

Scheme I·3



9 10 11 12

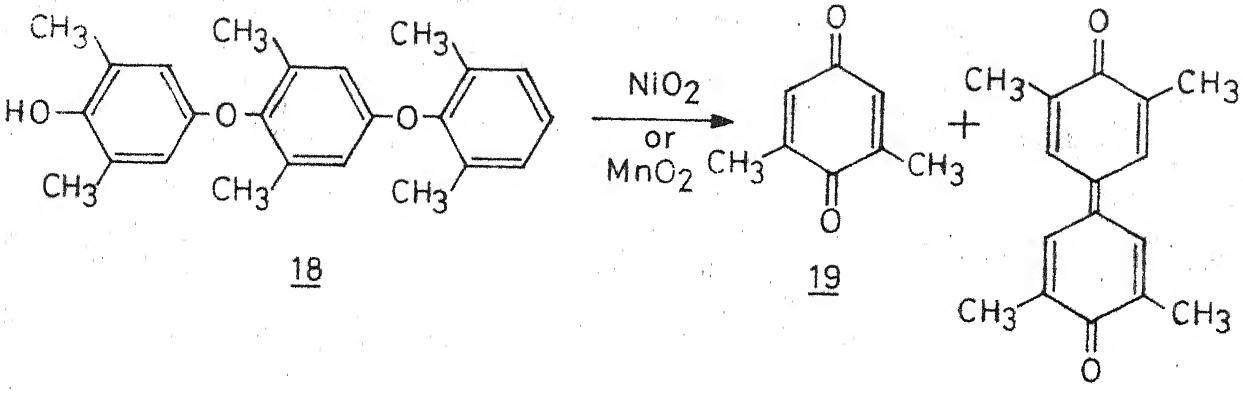
Scheme I·3 (Contd.)



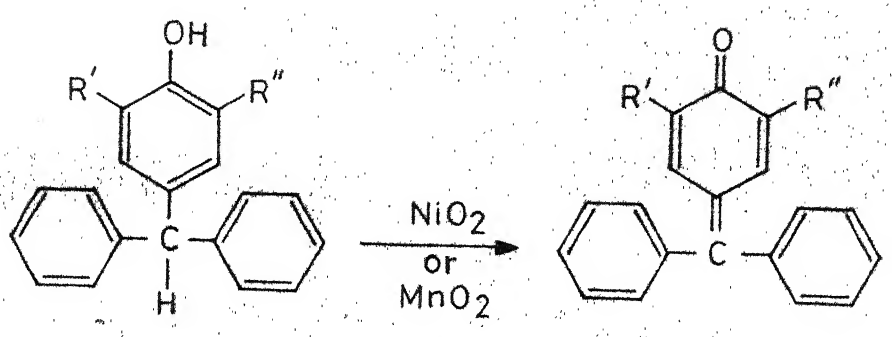
contrast, the manganese dioxide oxidation of 2,6-xylenol gives a mixture of both monomeric and dimeric products.[33] A tail-to-tail dimer, 2,2',6,6'-tetramethyl-4,4'-biphenol (16) is reported to be formed when a molar excess of xylenol is treated with the oxide. Also, a head-to-tail dimer, 4-(2,6-xylenoxy)-2,6-xylenol (17) is formed in the form of its oligomer which reacts further with the oxide to give a mixture of products consisting of a polymeric material, small amounts of 2,6-xylenol and the diphenoquinone, 15 (Scheme I.3). Similarly, 2,6-dimethyl benzoquinone,(19) and 3,3',5,5'-tetramethyl-4,4'-diphenoquinone (15) are obtained on oxidation of the xylenol trimer (18) with nickel peroxide,[34] as well as manganese dioxide (Scheme I.4).[34] 3,5-Disubstituted fuchsones (21) have been obtained on oxidation of the corresponding 3,5-disubstituted-4-hydroxytriphenylmethanes (20) with nickel peroxide or manganese dioxide (Scheme I.4).[35]

Treatment of p-chlorophenol with nickel peroxide in benzene yields polymers and oligomers.[35] Similarly, 2,6-dichlorophenol gives rise to poly-2,6-dichlorophenylene ether,[37] whereas, 2,4,6-trichlorophenol (22) gives a mixture of 2,6-dichloro-1,4-benzoquinone (23) and 2-chloro-6-(2,4,6-trichlorophenoxy)-1,4-benzoquinone (25) (Scheme I.4).[30] The reactions of o- and p-tert-butylphenols with nickel peroxide give polymeric products,[38] while 2,6-di-tert-butylphenol (26) gives a quantitative yield of 3,3',5,5'-tetra-tert-butyl-4,4'-diphenoquinone (27) (Scheme I.4).[31] An interesting reaction is observed in the case of the oxidation of catechol (28) which

Scheme I·4

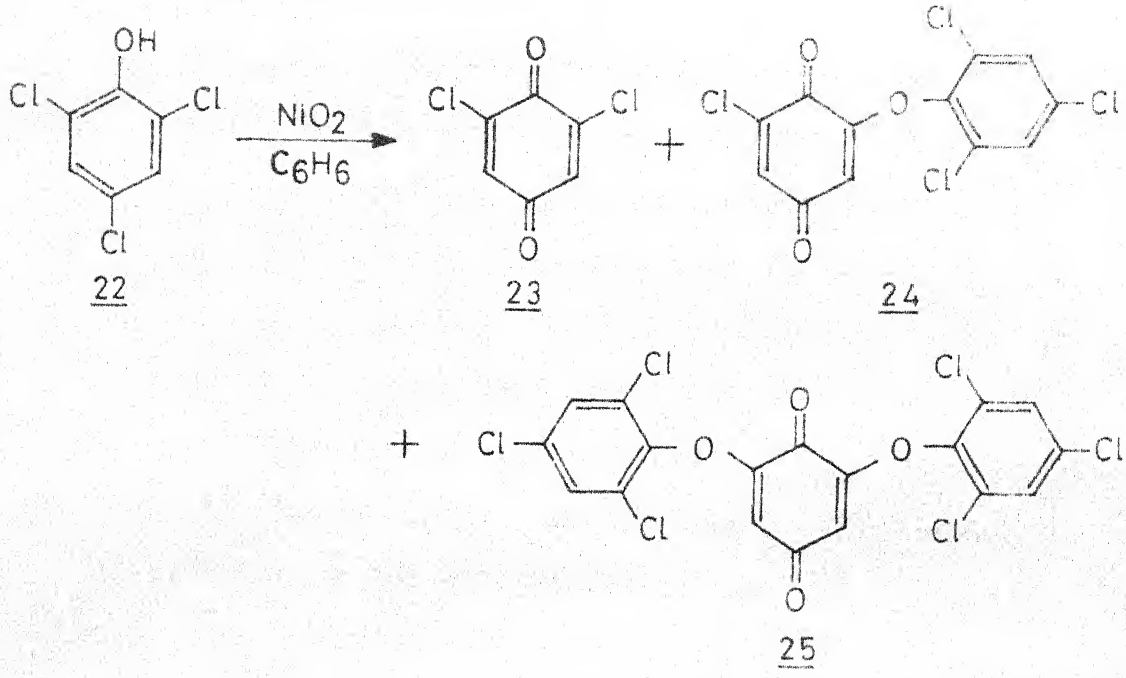


18 19 15



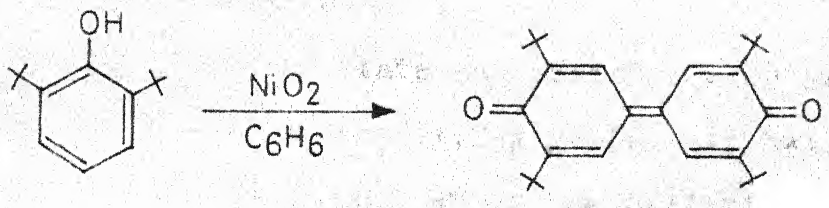
20 21

Scheme 1.4 (Contd.)

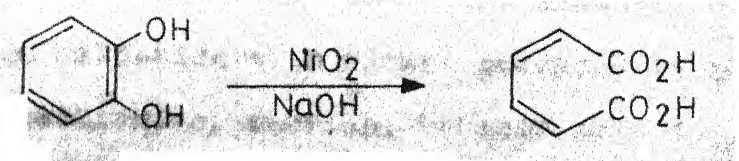


22 23 24

25



26 27



28 29

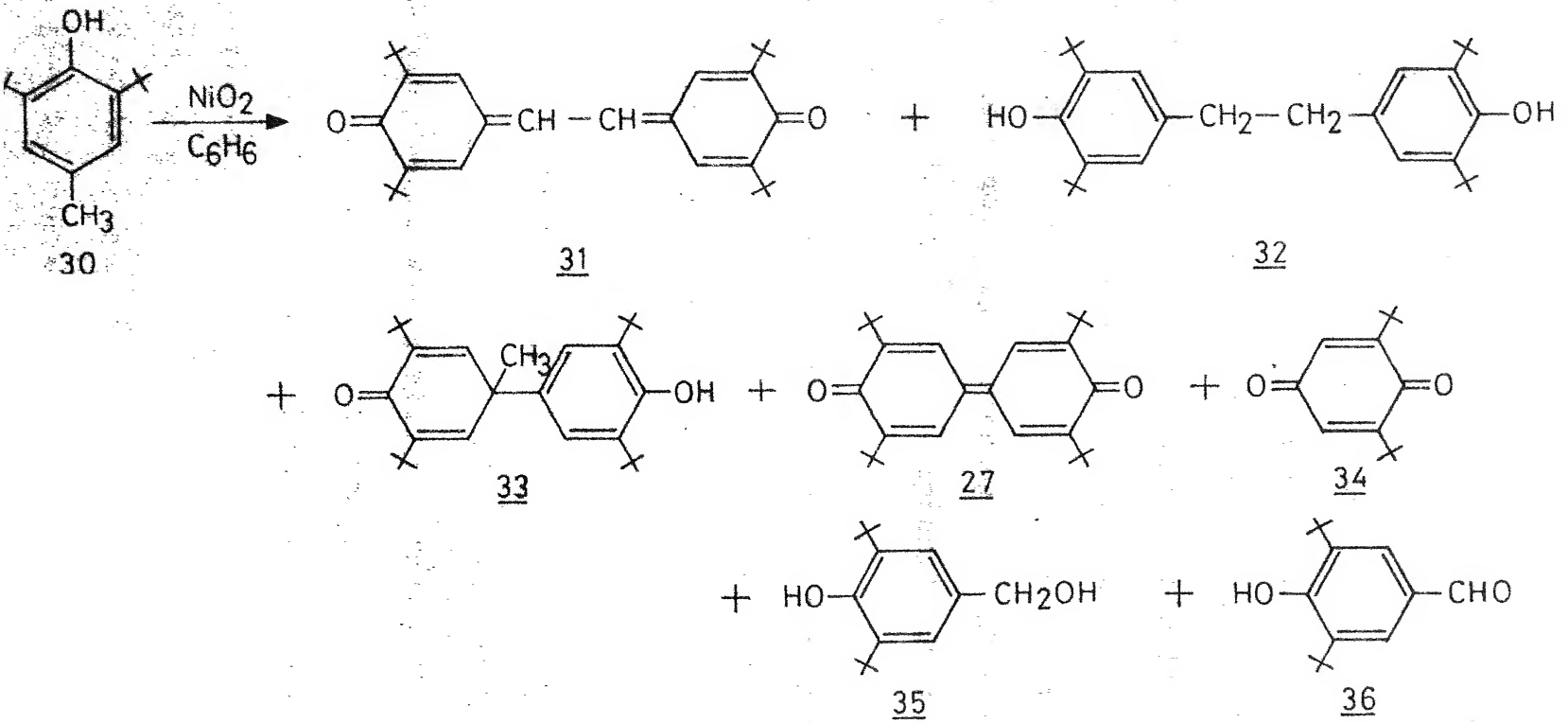
is converted by nickel peroxide in basic medium to cis,cis-muconic acid (29), arising through a fission of the aromatic ring (Scheme I.4).[39]

An unusual oxidative dealkylation has been reported in the case of 2,6-di-tert-butyl-4-methylphenol (30).[38] Treatment of 30 in benzene at room temperature with nickel peroxide gives a mixture of products, consisting of 27, 31, 32, 33, 34, 35 and 36 (Scheme I.5). A similar oxidative dealkylation is reported in the manganese dioxide oxidation of mesitol.[40] The oxidation of 4-cyanocatechol (37) is reported to give rise to an ortho-quinone intermediate which has been trapped in presence of 2,3-dimethylbutadiene (38) to give the adduct 39 (Scheme I.5).[41]

I.5 POLYHYDROXY COMPOUNDS

Lead tetraacetate and periodic acid are commonly employed in the cleavage of 1,2-glycols. It has been shown that nickel peroxide brings about the oxidation of a wide variety of polyhydroxy compounds such as α-glycols, α-hydroxy acids, α-oxo alcohols and α-oxo acids.[39] It is interesting to note that the oxidation in organic solvents give oxidative fragmentation products. Thus, for example, phenylethylene glycol on oxidation with nickel peroxide in benzene solution gives benzaldehyde, whereas, benzoic acid is formed as the only product, when the oxidation is carried out in aqueous medium. Similarly, cis-cyclohexanediol gives adipaldehyde in benzene medium. α-Hydroxy acids are reported to undergo oxidative decarboxylation. Mandelic acid, for example, gives

Scheme I·5


OH
CH3
NiO2
C6H6
30
O
CH
CH
O
31
HO
CH2
CH2
OH
32
CH3
O
OH
33
O
O
27
O
O
34
HO
CH2OH
35
HO
CHO
36
OH
OH
CN
37
CH3
CH3
38
NiO2
OH
CH3
CH3
O
CN
39

benzaldehyde on oxidation with nickel peroxide in benzene solution. In aqueous medium, however, the product formed is benzoic acid.[39] It might be mentioned in this connection that polyhydric alcohols like ethylene glycol, glycerol and mannitol have been reported to be oxidized to a mixture of carbon dioxide and water when boiled with a suspension of manganese dioxide in water. Vicinal glycols, and α-hydroxy acids undergo oxidative fission with manganese dioxide.[42] It has been suggested that in the nickel peroxide oxidation of 1,2-glycols, the abstraction of α-hydrogen atoms competes with the oxidative cleavage.[8] By comparing the rates of oxidation of meso-hydrobenzoin and meso-1,2-diphenyl-1,2-dideuteroethane-1,2-diol, it has been possible to show that no deuterium isotope effect is involved. Accordingly, it has been suggested that the oxidative cleavage of meso-hydrobenzoin occurs through a concerted process in which a non-cyclic nickel complex is involved.[8]

I.6 CARBONYL COMPOUNDS

Oxidation of aldehydes with nickel peroxide in alkaline medium gives rise to carboxylic acids.[10] Thus, benzaldehyde is converted smoothly to benzoic acid. Similarly, furfural is oxidized to furoic acid. Aldehydes containing α-hydrogen atoms, on the other hand, are reported to give aldol condensation products and this may be due to the alkalinity of the reaction mixture. Aromatic aldehydes are reported to give the corresponding carboxylic acids on treatment with manganese dioxide.[13]

An interesting oxidative dimerization has been reported in the nickel peroxide oxidation of iso-butyraldehyde (40) leading to the formation of a mixture of both C-C and C-O dimers 41 and 42, respectively (Scheme I.6).[43] The same oxidative dimerization has been observed with manganese dioxide also.[43]

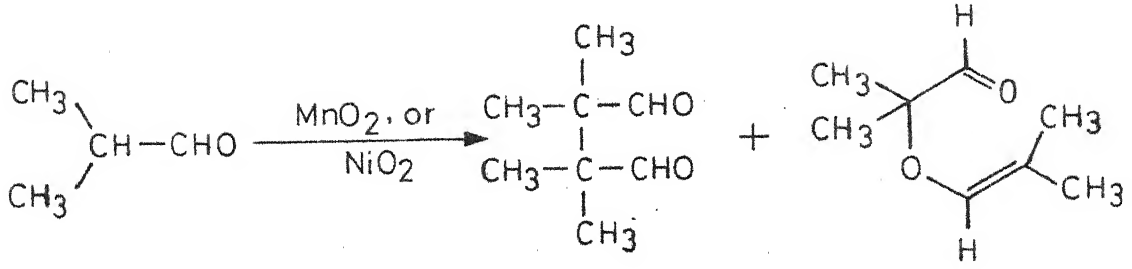
It has been reported that the oxidation of aldehydes with lead tetraacetate, in presence of ammonia, gives rise to nitriles.[44] Nakagawa and coworkers[45] have shown that alcohols and aldehydes can be directly converted to the corresponding amides, if the nickel peroxide oxidation is carried out in an ether solution containing ammonia at -20°. At higher temperatures, however, the yields of the amides are lower and the corresponding nitriles are formed as major products (Scheme I.7). Corey and coworkers[46] have recently reported that manganese dioxide in presence of sodium cyanide oxidizes aldehydes to the corresponding acids or esters, when the reaction is carried out in acetic acid or alcohol, respectively. Cyanohydrins are supposed to be the intermediates in these reactions which get oxidized to the corresponding acyl cyanides. These acyl cyanides are subsequently transformed to either acids or esters in presence of the appropriate solvents (Scheme I.8).

I.7 AMINES

I.7.1 Primary Amines

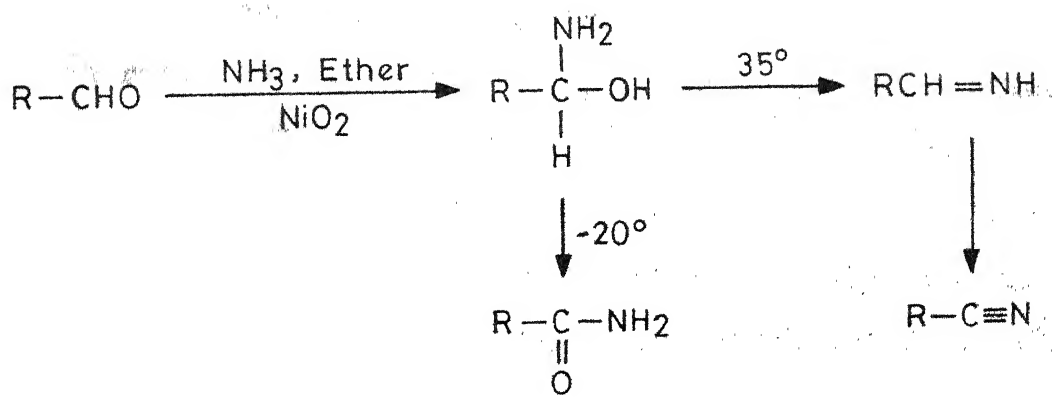
Aliphatic and aromatic primary amines are oxidized by both nickel peroxide[47] and manganese dioxide[13,15,48] and two modes of reactions have been observed in these cases.

Scheme I·6

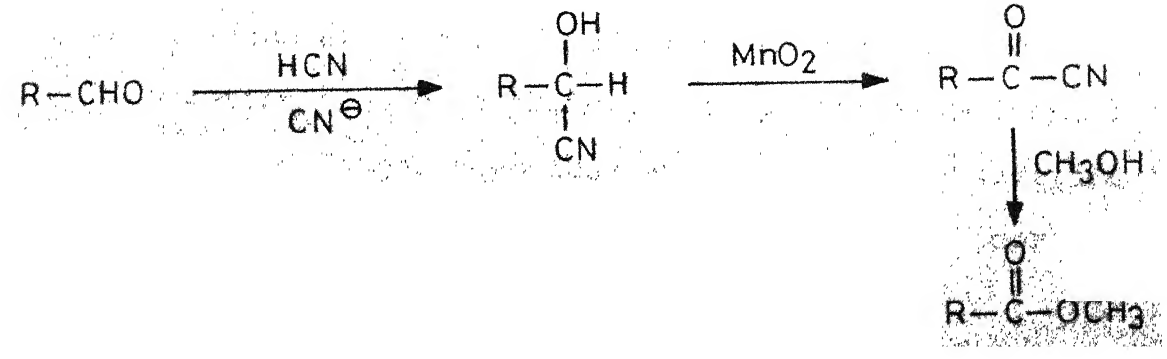


40 41 42

Scheme I·7



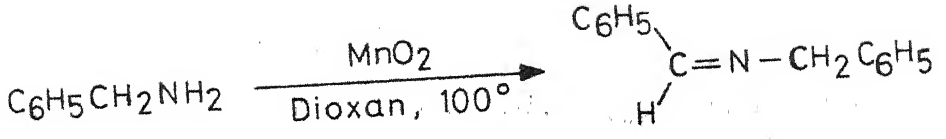
Scheme I·8



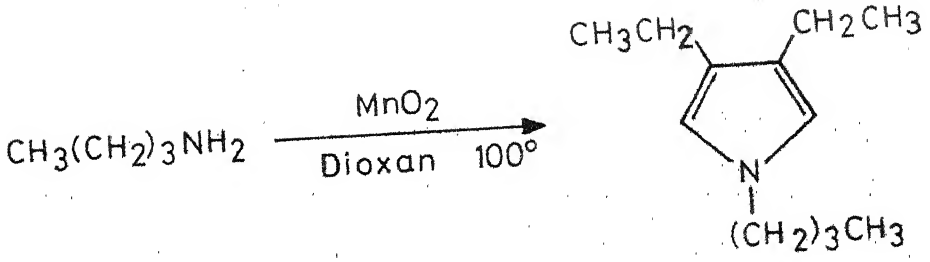
Aromatic primary amines are readily converted to the corresponding symmetrical azo compounds when oxidized either with nickel peroxide or manganese dioxide. Aliphatic primary amines, on the other hand, give rise to different products depending on the nature of the oxidizing agent. Thus, the oxidation of aliphatic primary amines with nickel peroxide gives rise to nitriles, whereas aldehydes are formed as major products, in the case of the manganese dioxide oxidation. It has been observed that benzylamine, furfurylamine and n-heptylamine are oxidized to the corresponding nitriles by nickel peroxide.[47] Highet and Wildman[48] have reported the isolation of imine intermediate in the manganese dioxide oxidation of benzylamine. A recent report, however, suggests that benzylidenebenzylamine (44) is formed on refluxing benzylamine (43) with manganese dioxide in dioxan.[49] Under similar conditions, butylamine (45) has been reported to give a cyclic product, 1-butyl-3,4-diethylpyrrole (46) (Scheme I.9).[49] Phenylethylamine (47), on oxidation with nickel peroxide gives trans-α,α'-stilbenedicarbonitrile (48) (Scheme I.9).[1]

A detailed study of the oxidation of aromatic primary amines with manganese dioxide has been made by Barakat and coworkers[13] who have found that nitroanilines are not oxidized readily to the corresponding azo compounds unlike other aromatic amines. However, the oxidation with nickel peroxide leads to the formation of azo compounds, without the formation of resinous materials.[47] It has been observed that in the oxidation of chloroanilines, anisidines and toluidines, only poor yields of

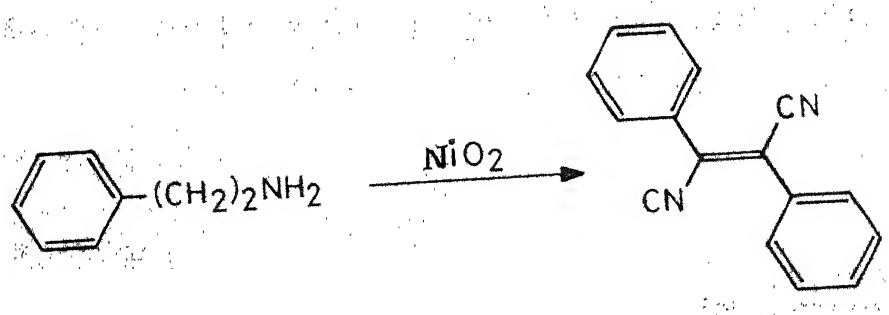
Scheme 1.9



43 44



45 46



47 48

the azo compounds are formed,[47] as compared to the manganese dioxide oxidation of these amines.

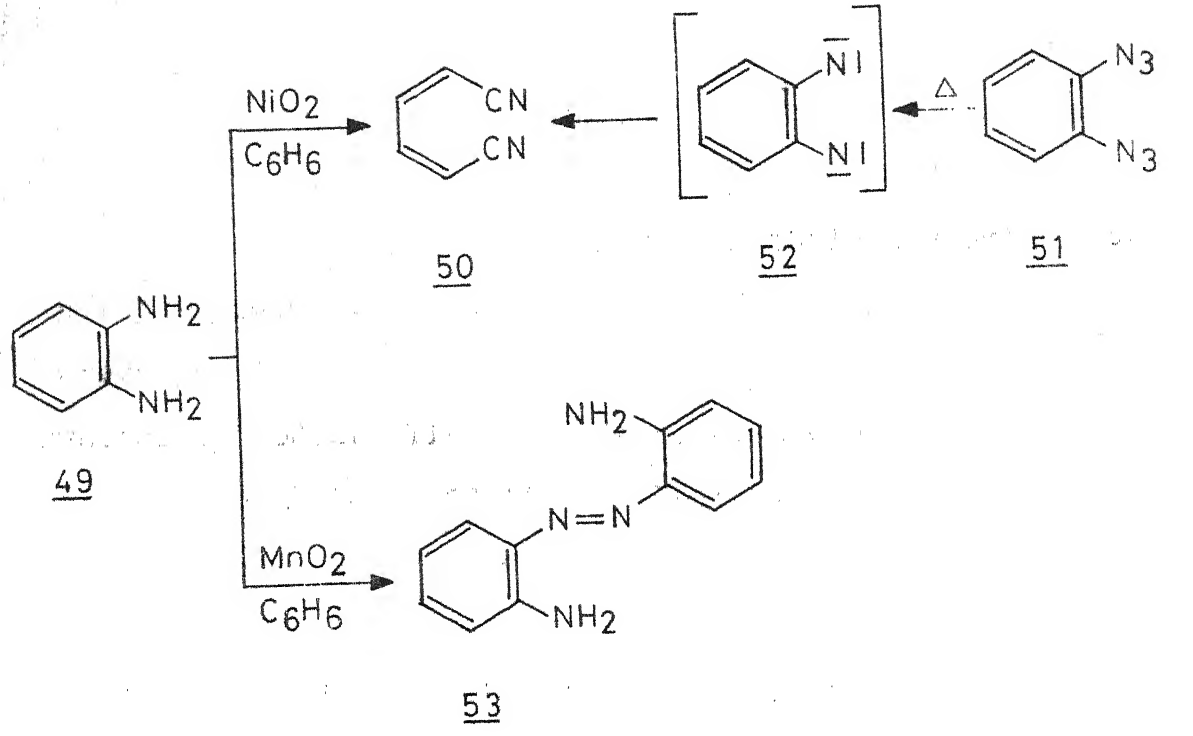
Nickel peroxide oxidation of o-phenylenediamine(49) results in the cleavage of the aromatic ring to give cis,cis-1,4-dicyano-1,3-butadiene (50) which has been characterized through its Diels-Alder adduct (Scheme I.10).[50] In contrast, the oxidation of o-phenylenediamine (49) with manganese dioxide gives 2,2'-diaminoazobenzene (53) (Scheme I.10).[52] Similarly, the oxidation of 1,2-diaminonaphthalene with nickel peroxide gives the corresponding dinitrile. However, the analogous dinitrile, could not be isolated from the nickel peroxide oxidation of 2,3-diaminonaphthalene. The formation of the dinitrile 50 in the oxidation of o-phenylenediamine (49) may be proceeding through the dinitrene intermediate (52), which is a reported intermediate in the thermal decomposition of 1,2-diazidobenzene (51) (Scheme I.10).[51]

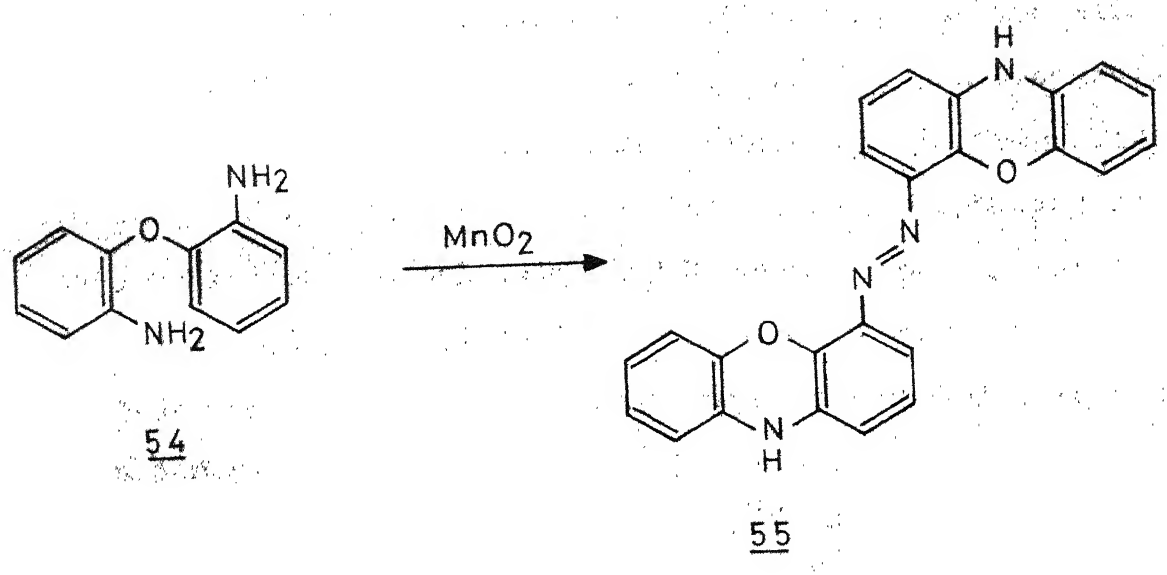
The manganese dioxide oxidation of 2,2'-diaminobiphenyl gives dibenzopyridazine, arising through an oxidative coupling.[52] In contrast, 2,2'-diaminobiphenyl ether (54) gives rise to the azo compound 55 (Scheme I.10), which involves both an oxidative cyclization and an oxidative coupling of the amino group.[53]

I.7.2 Secondary Amines

A secondary amine like diphenylamine (56), on oxidation with nickel peroxide yields tetraphenylhydrazine (57) and a polydiphenylamine (58) in which each nitrogen atom is bonded

Scheme I·10


NiO2
C6H6
MnO2
C6H6
NH2
NH2
CN
CN
N3
N3
Δ
Ni
Ni
N=N
49
50
52
51
53

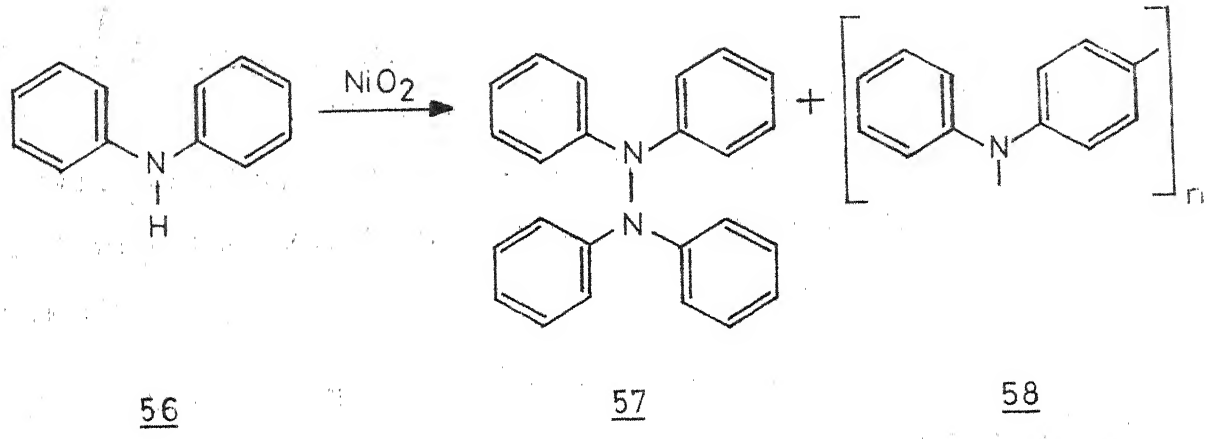

NH2
NH2
O
MnO2
H
N
O
N
N
O
N
H
54
55

to the para position of another diphenylamine molecule.[54] 4-Methyldiphenylamine (59) under similar conditions, gives the hydrazine derivative 60 and N-(p-tolyl)-p-benzoquinone monoimine (61) (Scheme I.11).[54] Similarly, the oxidation of carbazole (62) with nickel peroxide gives 9,9'-bicarbazole (63), 9,3',9',9''-tercarbazole (64) and some polymeric materials (Scheme I.11).[55]

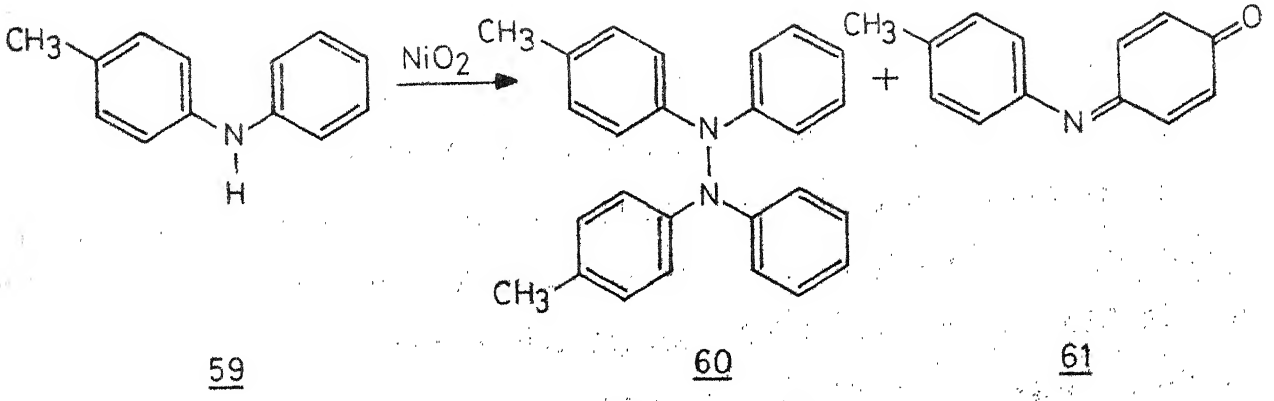
Secondary amines like N-methylbenzylamine and N-methylpiperonylamine are reported[56] to give rise to the corresponding imines when oxidized with manganese dioxide, whereas, products like formaldehyde, acetaldehyde and azobenzene are formed in the oxidation of N-ethylaniline.[57]

Manganese dioxide oxidation of N-benzylanilines has been reported to give rise to the corresponding benzylideneanilines.[58] On the contrary, nickel peroxide oxidation gives two types of oxidative dimers, in addition to benzylideneanilines.[59] Thus, N-benzylaniline (65), on oxidation with nickel peroxide gives benzylideneaniline (66) and N-benzyl-N-phenyl-N'-benzylidene-p-phenylenediamine (67) (Scheme I.12).[59] Similarly, N-benzyl-o-toluidine gives the corresponding Schiff's base, benzylidene-o-toluidine and N-benzyl-N-o-tolyl-N'-benzylidene-2-methyl-p-phenylenediamine. On the other hand, the oxidation of N-benzyl-p-toluidine (68) with nickel peroxide gives benzylidene-p-toluidine (69) and N,N'-dibenzyl-N,N'-di-p-tolyl-hydrazine (70) (Scheme I.12).[59] Likewise, N-benzyl-p-chloroaniline gives the corresponding Schiff's bases and hydrazine derivatives. The oxidation of dibenzylamine (71)

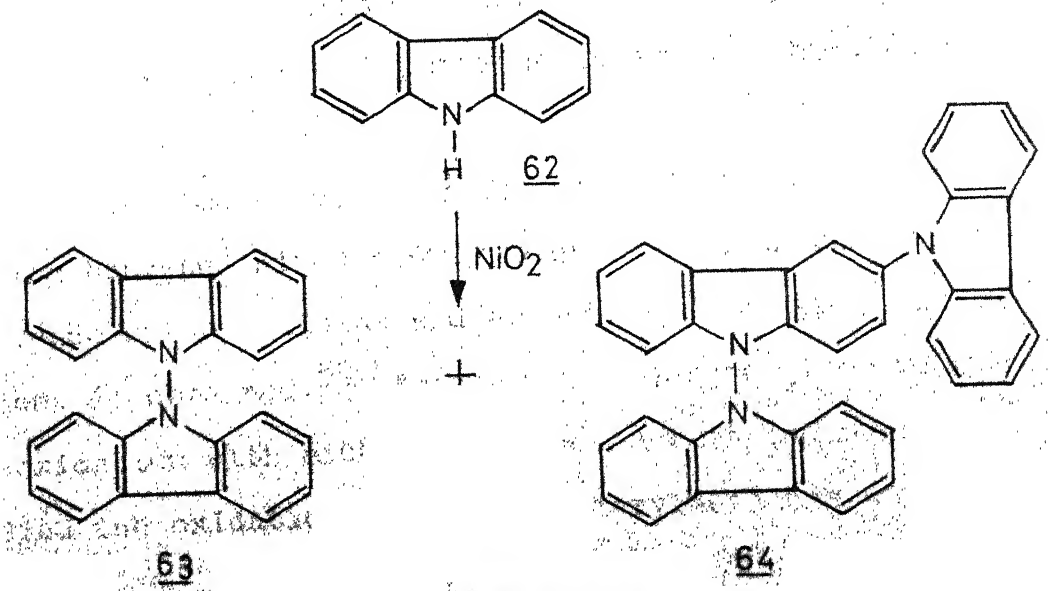
Scheme I·11



56 57 58



59 60 61



+ Polymers

yields a mixture of N-benzylidenebenzylamine (44), benzaldehyde (72) and benzonitrile (73) (Scheme I.12).[59]

I.7.3 Tertiary Amines

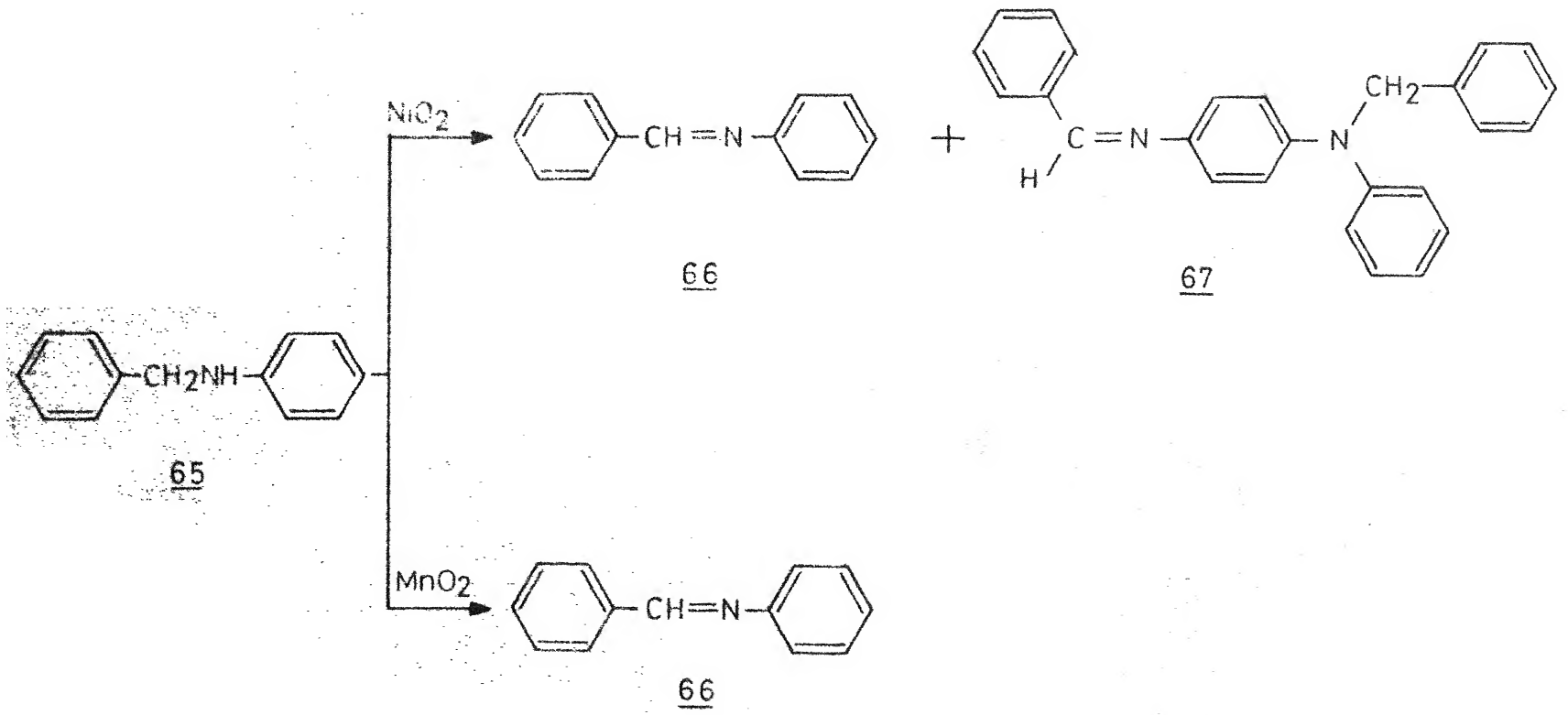
Tertiary amines have so far not been oxidized by nickel peroxide, whereas, numerous reports have appeared which deal with the oxidation of these compounds using manganese dioxide.[62]

I.8 COMPOUNDS CONTAINING ACTIVATED C-H BONDS

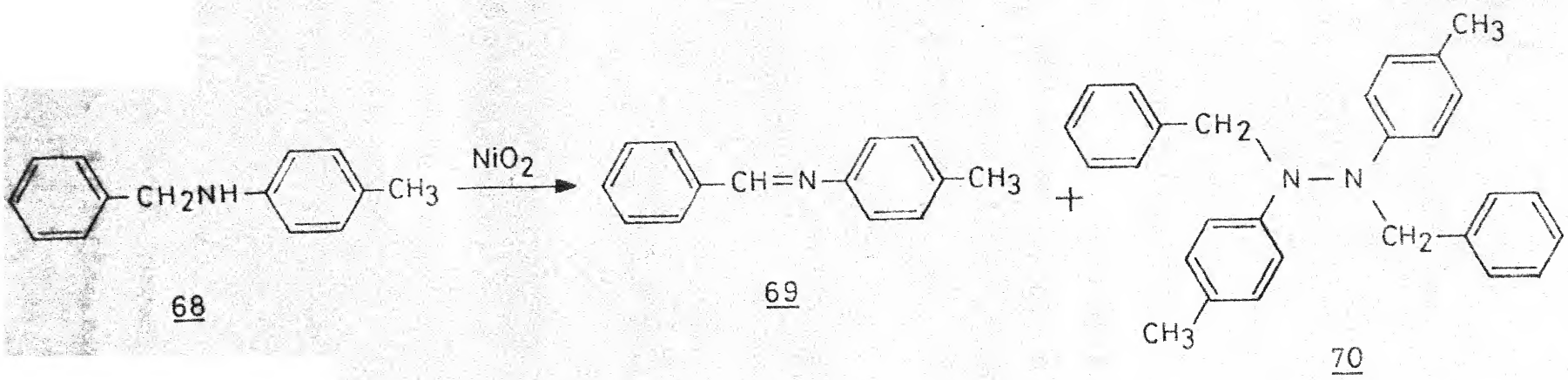
Nickel peroxide oxidation of hydrocarbons containing activated C-H bonds is extremely slow under mild conditions, while under drastic conditions, these hydrocarbons are oxidized to the corresponding carboxylic acids.[1] In the oxidation of toluene, for example, further addition of nickel peroxide after 8 hr results in an increased yield of benzoic acid. Manganese dioxide, on the other hand, does not oxidize simple hydrocarbons like toluene, xylene and ethylbenzene. In the cases of cumene and bibenzyl, the yield of benzoic acid is low compared to the nickel peroxide case. Thus, it appears that the oxidizing power of nickel peroxide is greater than that of manganese dioxide.

Diphenylmethane, on oxidation with nickel peroxide in refluxing benzene,[1] gives a 56% yield of benzophenone, whereas in the absence of any solvent and around 110°, a 79% yield of benzophenone is obtained.[59] Similarly, fluorene gives fluorenone on oxidation with nickel peroxide. Pratt and Suskind[60] have studied the oxidation of several diarylmethanes with

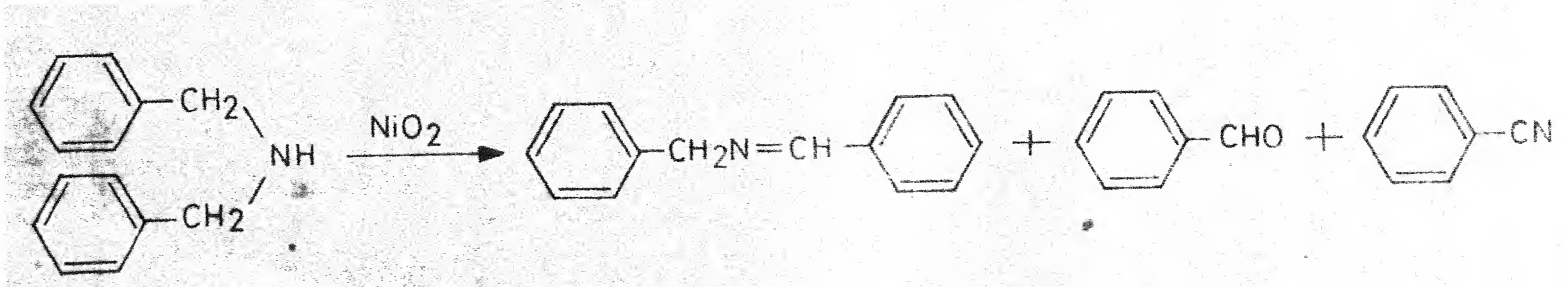
Scheme I-12



Scheme I·12 (Contd.)



68 69 70



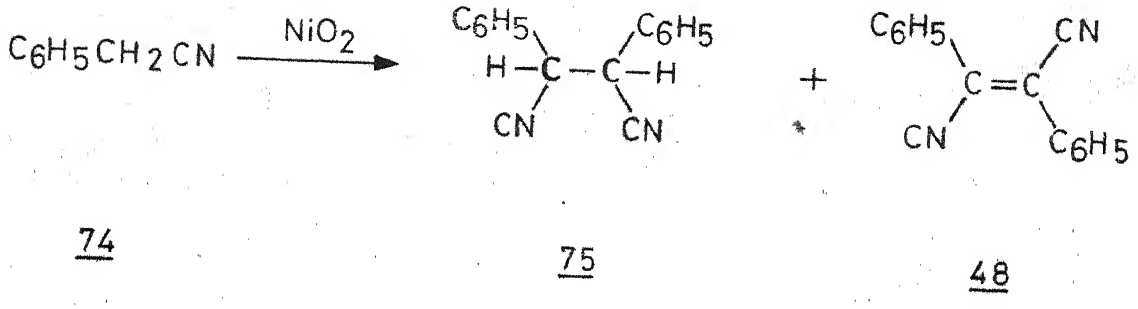
71 44 72 73

manganese dioxide and they have shown that different products are formed in these reactions, depending on the reaction conditions. Thus, diphenylmethane on oxidation in a mixture of refluxing benzene and biphenyl gives tetraphenylethane as the only product, whereas, in the absence of any solvent around 120°, benzophenone is formed in appreciable amounts.[60] Similarly, fluorene gives 9,9'-bifluorenylidene on treatment with manganese dioxide.[60]

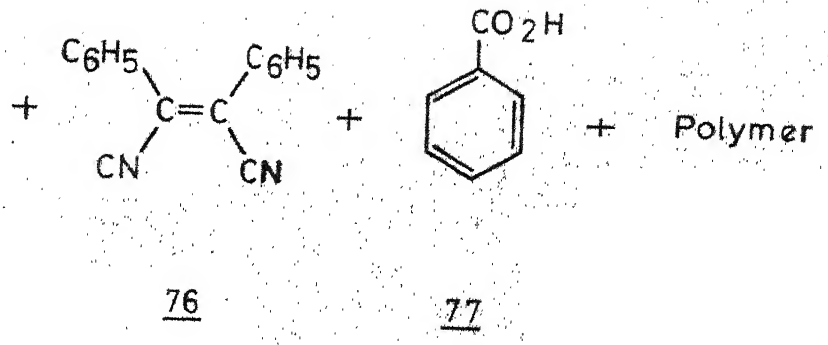
Tetraphenylsuccinonitrile is formed in quantitative amounts on treatment of diphenylacetonitrile with nickel peroxide for 1 hr.[1] Under analogous conditions, a 94% yield of tetraphenylsuccinonitrile is formed after treatment with manganese dioxide for 5 hr.[1]

The oxidation of phenylacetonitrile (74) with nickel peroxide[61] gives a mixture of products consisting of meso- and dl-2,3-diphenylsuccinonitrile (75), trans-dicyanostilbene (48), cis-dicyanostilbene (76) and benzoic acid (77) along with polymeric materials. The oxidation of meso-2,3-diphenylsuccinonitrile (75) itself leads to the same mixture of cyanostilbene 48 and 76 (Scheme I.13), together with polymeric materials.[61] On the other hand, active manganese dioxide does not oxidize phenylacetonitrile.[61] Oxidation of triphenylmethane with nickel peroxide results in the formation of triphenylcarbinol in poor yields.[6] In contrast, 9,10-dihydroanthracene is readily oxidized to anthracene, on treatment with nickel peroxide. In addition, a small amount of anthraquinone is also formed in this reaction. An interesting oxidative coupling reaction has been

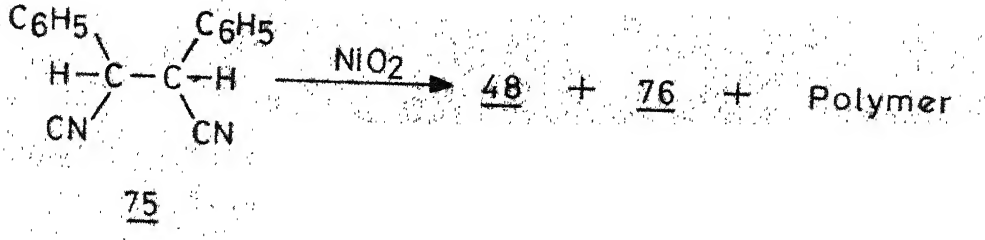
Scheme I.13



74 75 48

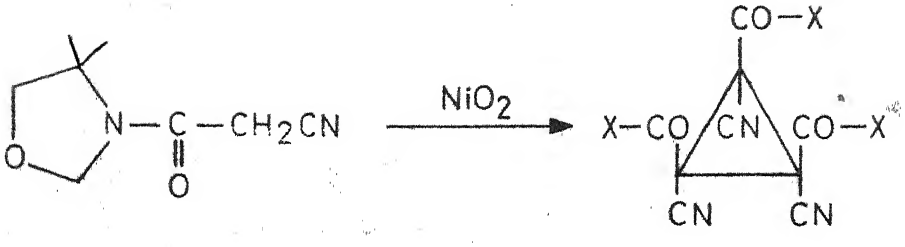


76 77

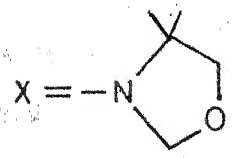


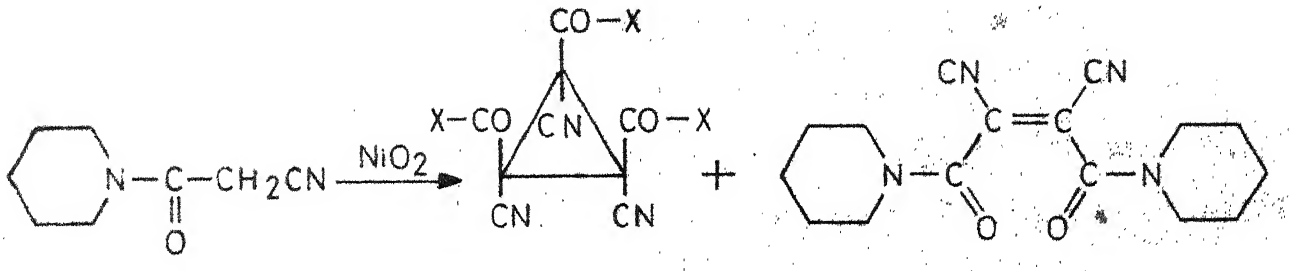
75

Scheme I·13 (Contd.)

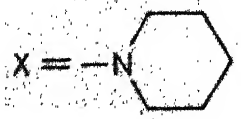


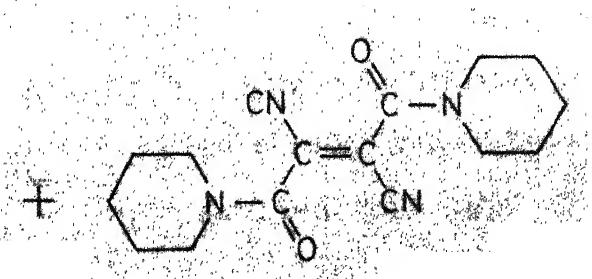
78 79





80 81 82





83

observed on treatment of N-(cyanoacetyl)-4,4-dimethyloxazolidine (78) with nickel peroxide, resulting in the formation of the cyclopropane derivative 79 (Scheme I.13).[62] In contrast, N-(cyanoacetyl)-piperidine (80) gives the cyclopropane derivative 81 and two isomeric 82 and 83, respectively (Scheme I.13).[62]

I.9 HETEROCYCLES

The dehydrogenation of heterocycles has been carried out using both nickel peroxide[59] and manganese dioxide.[2c] Pyrazolines are dehydrogenated by these reagents to give pyrazoles in excellent yields. Manganese dioxide has been more extensively used for these types of reactions as compared to nickel peroxide.[2]

I.10 TELOMERIZATION AND POLYMERIZATION REACTIONS

It has been observed that chloroform is converted to hexachloroethane in presence of nickel peroxide and the reaction is assumed to proceed through trichloromethyl radicals.[10] Such halogenated alkyl radicals formed in similar oxidation reactions have been used in different telomerization and polymerization reactions.[63,64] Thus, it has been observed that in the reaction of 1-octene with bromoform in presence of nickel peroxide, a 1:1-addition product is formed. However, styrene in presence of chloroform yields products with a higher degree of polymerization. Under analogous conditions, tetrabromomethane gives a 1:1-addition product in nearly quantitative yields. Tanaka and coworkers[65] have applied this type of

telomerization reaction to the synthesis of terpenes, ∝-terpineol, linalool, myrcene and dipentene by treating isoprene and prenyl chloride with nickel peroxide as initiator.[65] In a reaction similar to the telomerization reaction, a mixture of 2,2,2-trichloro-1,1,1-tribromoethane, hexachloroethane and hexabromoethane and tetrabromoethylene is formed on treatment of a mixture of chloroform, bromoform and carbon tetrachloride with nickel peroxide.[66] Nickel peroxide has also been employed in the synthesis of stereospecific polymers.[67-76]

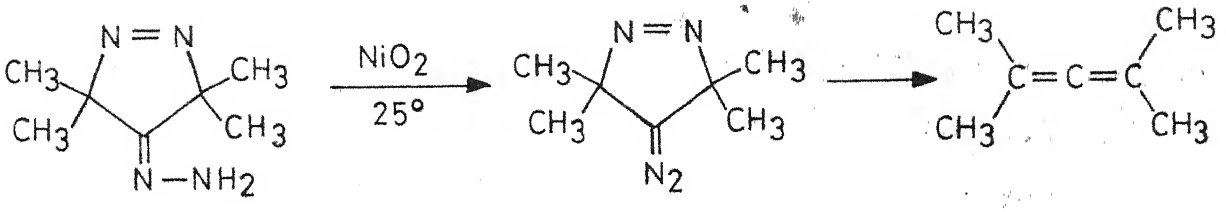
I.11 HYDRAZONES AND PHENYLHYDRAZONES

Hydrazones have been oxidized using both nickel peroxide and manganese dioxide. Nickel peroxide oxidation[77] of benzophenone hydrazone yields diphenyldiazomethane in nearly quantitative amounts, whereas, the reaction with manganese dioxide[78] gives diphenyldiazomethane contaminated with small amounts of diphenylketazine. Similarly, other aldehyde and ketone hydrazones such as benzaldehyde hydrazone, fluorenone hydrazone, diethyl mesoxalate hydrazone and acetone hydrazone are readily oxidized to the corresponding diazo compounds on treatment with nickel peroxide.[77] Barakat and coworkers[13] have observed that fluorenone hydrazone on treatment with manganese dioxide is converted to the corresponding azine. Aldehyde and ketone hydrazones, on the other hand, are oxidatively hydrolysed to the corresponding carbonyl compounds.[79] It has been assumed that diazo compounds are involved as intermediates in these reactions.

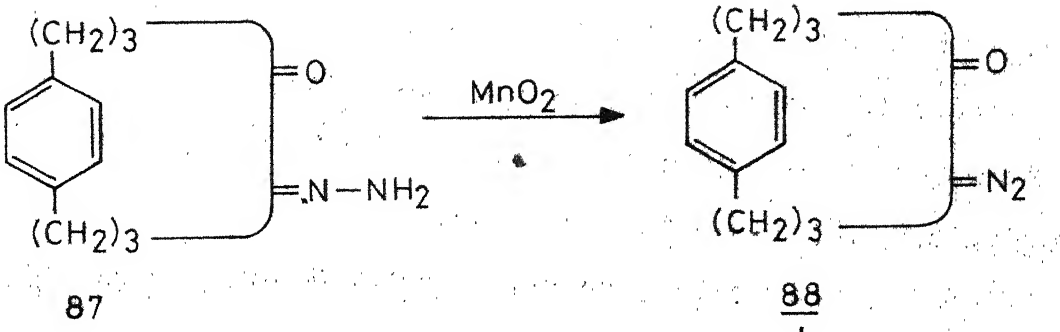
Oxidation of benzil monohydrazone with nickel peroxide[1] around 0° is reported to give a nearly quantitative yield of the α-diazoketone, whereas, the room temperature oxidation leads to a mixture of benzophenone and diphenylketone. Manganese dioxide oxidation of 1,2-diketone monohydrazones, similarly, gives rise to the corresponding α-diazoketones.[80,81] The oxidation of a pyrazoline hydrazone such as 4-ketone-3,3,5,5-tetramethylpyrazoline hydrazone (84) with nickel peroxide has been reported to give rise to tetramethylallene (86).[82] It has been suggested that the diazoalkane intermediate (85) is involved as an intermediate in this reaction (Scheme I.14). Similarly, the oxidation of a paracyclophane-1,2-diketone monohydrazone derivative 87 is oxidized to the corresponding diazoketone 88 with manganese dioxide which is finally converted to the carboxylic acid 89 (Scheme I.14).[83] 1,2-Diketonebishydrazones have been oxidized by both manganese dioxide and nickel peroxide to the corresponding alkynes. Thus, the oxidation of benzil bishydrazone with either nickel peroxide[1] or manganese dioxide[79] leads to the formation of tolan. Similarly, the oxidation of cyclohexane-1,2-dione bishydrazone with manganese dioxide gives cyclohexyne as the product.[84-86]

The oxidation of few aldehyde and ketone phenylhydrazones has been studied using both manganese dioxide and nickel peroxide. Thus, benzophenone phenylhydrazone on oxidation with manganese dioxide in benzene medium is converted to a mixture of benzophenone and biphenyl.[87] Nickel peroxide also

Scheme I·14



84 85 86



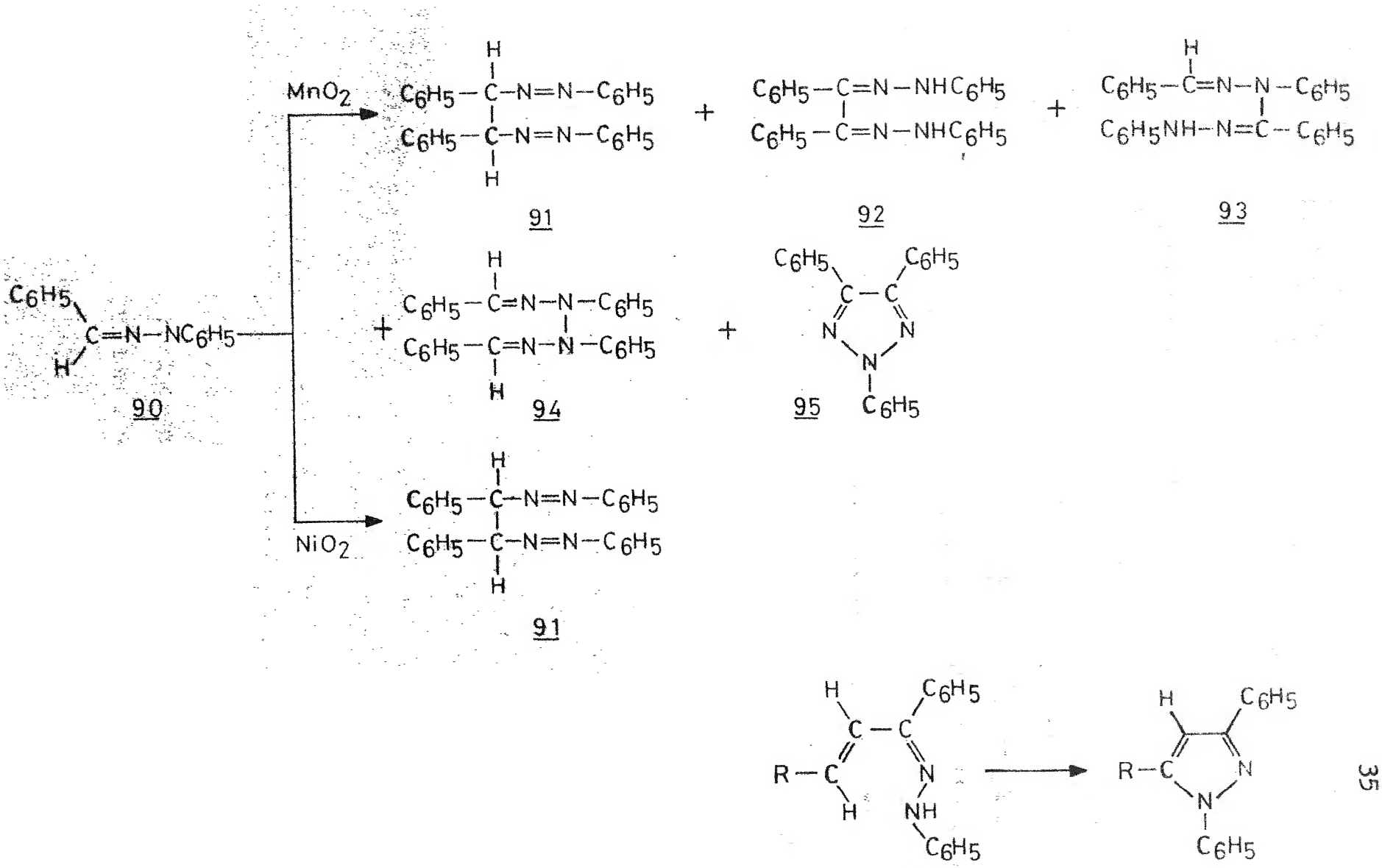
87 88 89

brings about the same transformation.[59] Oxidation of aldehyde phenylhydrazones, on the other hand, leads to a mixture of products. Benzaldehyde phenylhydrazone (90) on oxidation with manganese dioxide is converted to a mixture of 2,4,5-triphenyl-1,2,3-triazole (95) and several oxidative dimers consisting of 1,2-(bisphenylazo)-1,2-diphenylethane (91), benzil osazone (92), N^{α},$N^{\beta'}$-diphenyl-N^{β}-benzalbenzhydrazine (93) and 2,3-diphenyl-1,4-dibenzyltetrazene (94) (Scheme I.15).[87] Nickel peroxide oxidation of benzaldehyde phenylhydrazone (90), on the contrary, leads to the formation of only the C-C coupling product, 91.[59] Chalcone phenylhydrazones are oxidized by both nickel peroxide[59] and manganese dioxide[88] to give pyrazole derivatives (Scheme I.15).

I.12 HYDROXYLAMINES AND OXIMES

Aromatic hydroxylamines are oxidized to the corresponding azoxy compounds by nickel peroxide.[89] Thus, the oxidation of phenylhydroxylamine (96) with nickel peroxide gives azoxybenzene (98) (Scheme I.16). Similarly, 4-chlorophenylhydroxylamine, naphthylhydroxylamine and 4-methylnaphthylhydroxylamine give 4,4'-dichloroazoxybenzene, azoxynaphthalene and 4,4'-dimethylazoxynaphthalene, respectively. It is assumed that the nitroso compounds formed on the surface of the oxidant react further with hydroxylamine leading to the formation of azoxy compounds. Manganese dioxide has not been used for the oxidation of hydroxylamine derivatives except in the case of phenylhydroxylamine. Nitrosobenzene (97) has been reported to be formed when phenylhydroxylamine (96) is oxidized with

Scheme I·15



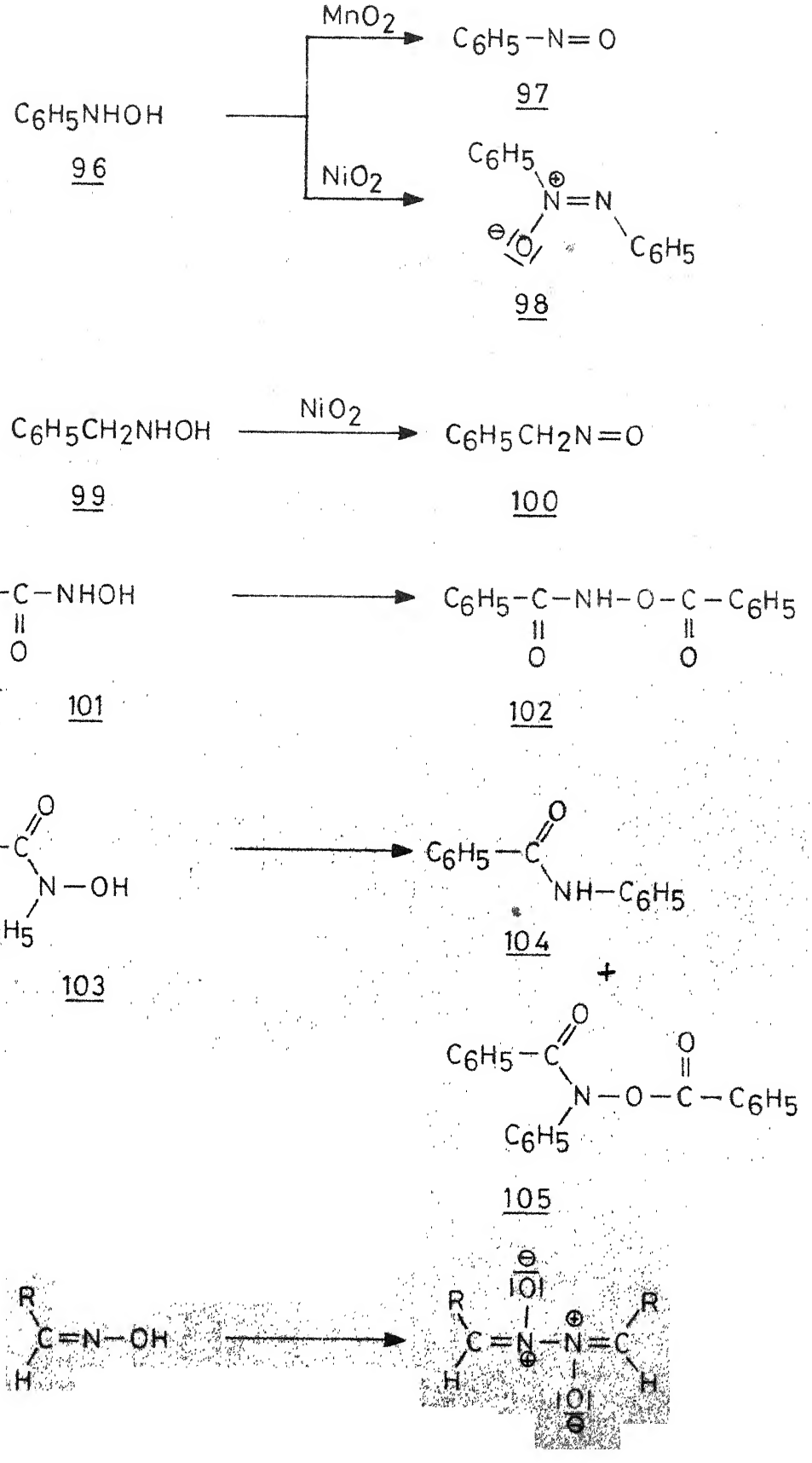
manganese dioxide (Scheme I.16).[90] Oxidation of N-benzylhydroxylamine (99) with nickel peroxide gives α-nitrosotoluene (100). The oxidation of benzohydroxamic acid (101) gives N,O-dibenzoylhydroxylamine (102) as the major product, whereas, N-benzoyl-N-phenylhydroxylamine (103) gives benzanilide (104) together with a small amount of N,O-dibenzoyl-N-phenylhydroxylamine (105) (Scheme I.16).[89] Aurich and Baer[7] have studied the nickel peroxide oxidation of N-acyl-N-phenylhydroxylamines and have shown through esr studies that acyl phenyl nitroxides are formed in these cases. They have suggested a free radical pathway for these oxidations.[7] The oxidation of aromatic aldoximes with nickel peroxide gives aldazine bis-N-oxides as major products (Scheme I.16).[1]

I.13 MISCELLANEOUS REACTIONS

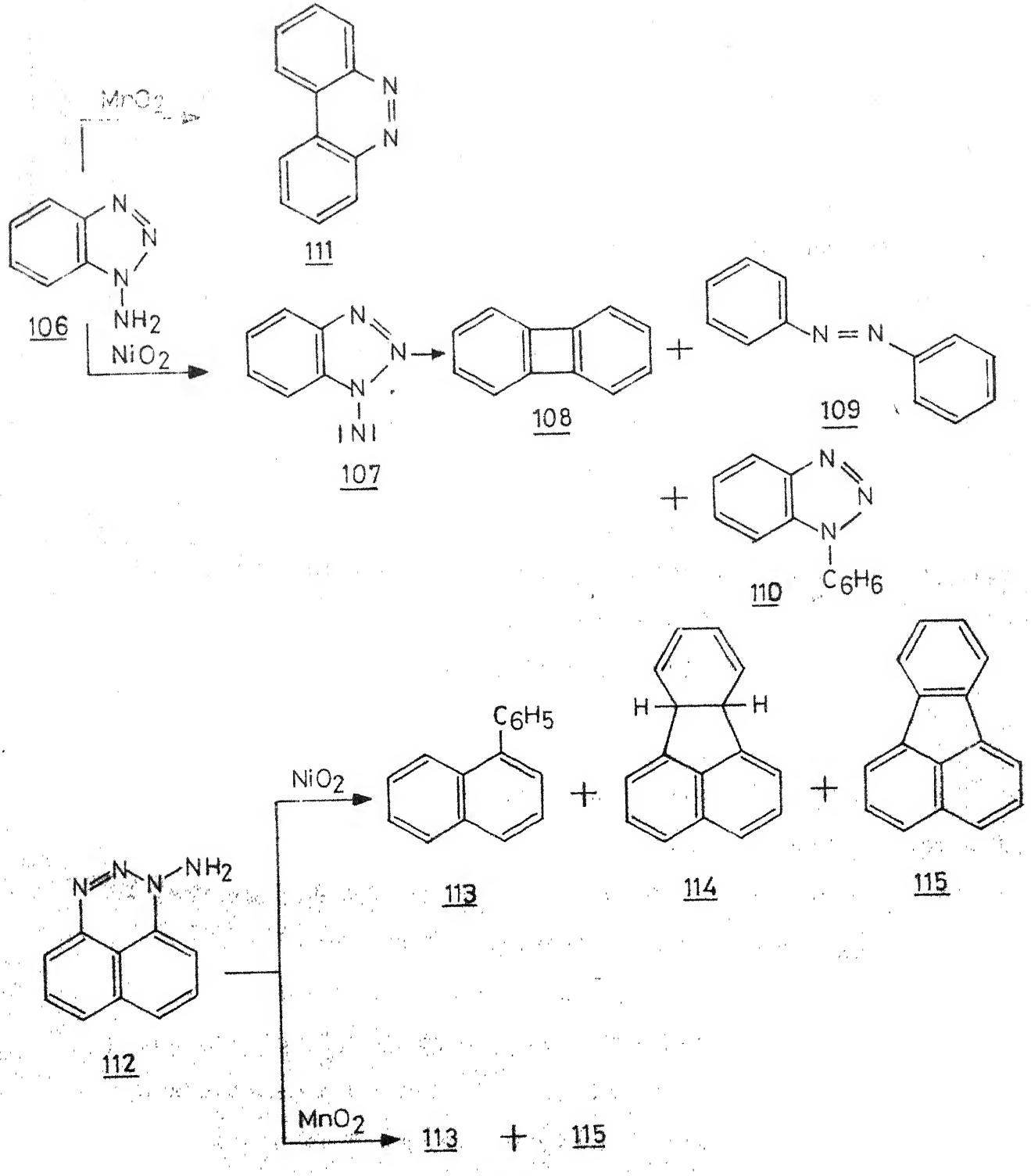
I.13.1 Aminotriazoles

The oxidation of 1-aminobenzotriazole (106) with nickel peroxide[91,92] gives a mixture of products consisting of biphenylene (108), azobenzene (109) and 1-phenylbenzotriazole (110), whereas, with manganese dioxide,[91] dibenzopyridazine (111) is the major product (Scheme I.17). It has been suggested that this oxidation proceeds through a nitrene intermediate 107 which fragments further, leading to various products. In contrast, the oxidation of 1-aminonaphtho-[1,8-d,e]-triazine (112) with nickel peroxide gives a mixture of 1-phenylnaphthalene (113), 6b, 10a-dihydrofluoranthene (114) and fluoranthene (115).[93] Under analogous conditions, only traces of 113 and 114 are formed in the manganese dioxide oxidation of 112 (Scheme I.17).[93]

Scheme I·16


MnO2
C6H5–N=O
97
C6H5NHOH
96
NiO2
C6H5
N=N
C6H5
98
C6H5CH2NHOH
NiO2
C6H5CH2N=O
99
100
C6H5–C–NHOH
C6H5–C–NH–O–C–C6H5
101
102
C6H5–C–N–OH
C6H5
103
C6H5–C–NH–C6H5
104
+
C6H5–C–N–O–C–C6H5
C6H5
105
R
C=N–OH
H

Scheme I 17


MnO2
NH2
NiO2
106
111
107
108
109
110
C6H6
C6H5
H
H
112
113
114
115
NiO2
MnO2
113 + 115

I.13.2 Sulfur Compounds

Thiophenol and ethyl mercaptan are easily oxidized to their corresponding disulfides in good yields on treatment with nickel peroxide.[94] Oxidation of sulfides to sulfones, however, appears to proceed very solwly. Diphenyl sulfide, for example, on oxidation with nickel peroxide under drastic conditions gives the corresponding sulfone.[94] On the other hand, diphenylene sulfide is unaffected on treatment with nickel peroxide. In contrast, manganese dioxide oxidizes mercaptans to disulfides and sulfides to sulfoxides.[95]

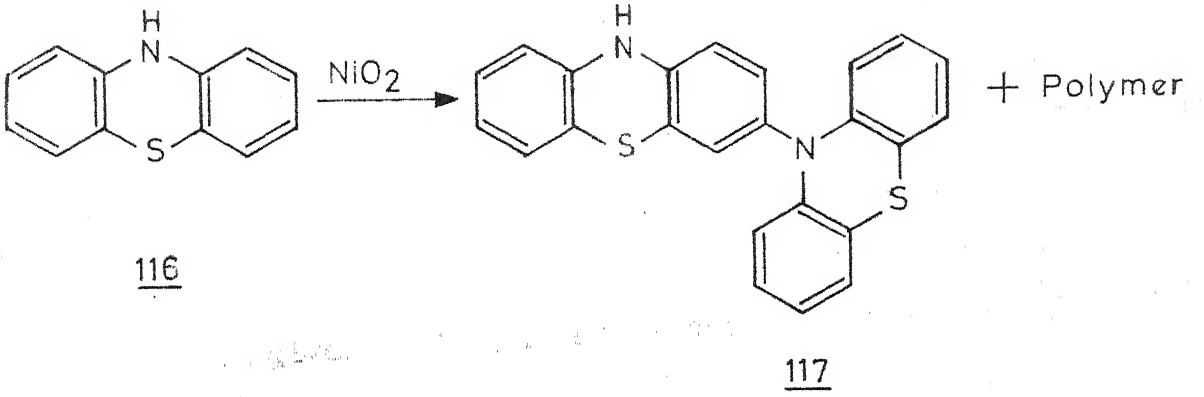
I.13.3 Schiff's Bases

Schiff's bases, prepared from substituted o-aminophenols and benzaldehyde, undergo oxidative cyclization with nickel peroxide[97] as well as manganese dioxide[88,98,99] to form 2-phenylbenzoxazole derivatives in good yields.

I.13.4 Phenothiazines

Phenothiazine (116) is oxidized by nickel peroxide to give 3,10'-biphenothiazine (117) and a polymeric material.[100] Similarly, 2-chloro-and 4-chlorophenothiazines give polymeric products. In contrast, 10-methylphenothiazine (118) gives a mixture of 10-methylphenothiazine-5-oxide (119), 10-methylphenothiazine-5,5-dioxide (120), 3H-phenothiazine-3-one (121) and a polymeric product.[99] Similarly, 2-chloro-10-methylphenothiazine has been reported to give 5-oxide, 5,5-dioxide and 2-chlorophenothiazine while 4-chloro-10-methylphenothiazine gives the 5-oxide and 4-chlorophenothiazine (Scheme I.18).[100]

Scheme I·18



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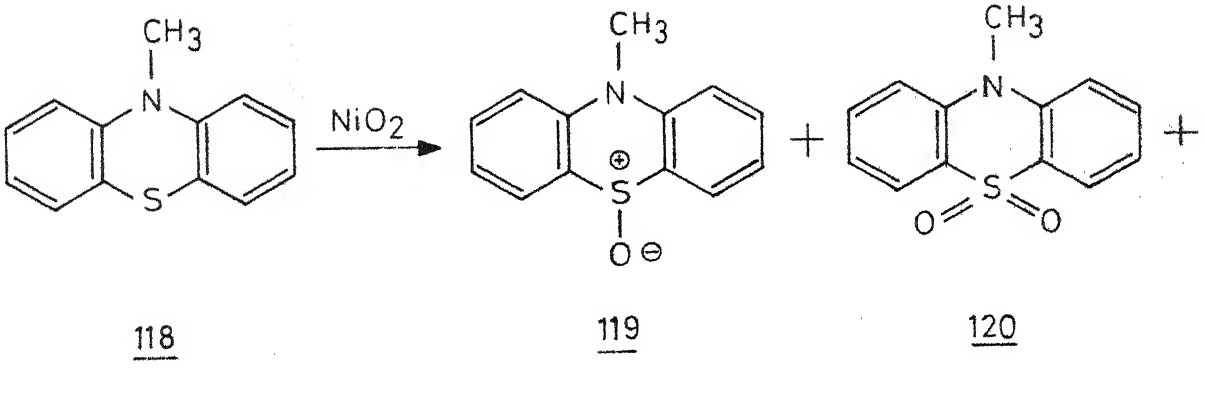

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I.13.5 Phenylhydrazine

Phenylhydrazine has been oxidized with nickel peroxide to give different products depending on the nature of the solvent employed.[101] Thus, the oxidation of phenylhydrazine with nickel peroxide in cyclohexane gives benzene and biphenyl, whereas, chlorobenzene, benzene, biphenyl and hexachloroethane are the products isolated, when carbon tetrachloride is used as the solvent. In benzene medium, the products of oxidation are biphenyl, traces of phenol and 1,4-dihydrobiphenyl. In contrast, the oxidation of phenylhydrazine with manganese dioxide, in benzene, gives biphenyl and azobenzene.[52]

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CHAPTER II

OXIDATION OF BENZYLIDENE-ACETONE PHENYLHYDRAZONE WITH NICKEL PEROXIDE.[1]

II. 1 ABSTRACT

Benzylideneacetone phenylhydrazone on oxidation with nickel peroxide gives a dl-mixture of 1,1',5,5'-tetraphenyl-3,3'-dimethyl-4,4'-bipyrazoline, whereas, 2-methylbenzylideneacetone phenylhydrazone under similar conditions, gives meso-1,1'-diphenyl-3,3'-dimethyl-5,5'-di-(o-tolyl)-4,4'-bipyrazoline. Similarly, meso-4,4'-bipyrazolines are formed in the oxidation of 2-chloro- and 4-methylbenzylideneacetone phenylhydrazones and furfurylideneacetone phenylhydrazone. A mixture of both dl- and meso- forms of 4,4'-bipyrazolines, however, is obtained in the oxidation of 3-chloro-, 4-chloro- and 3-methylbenzylideneacetone phenylhydrazones and piperonylideneacetone phenylhydrazone. The ir and nmr spectra of both the dl- and meso- forms of 4,4'-bipyrazolines have been discussed. Mass spectral fragmentation of some of these pyrazolines has also been examined.

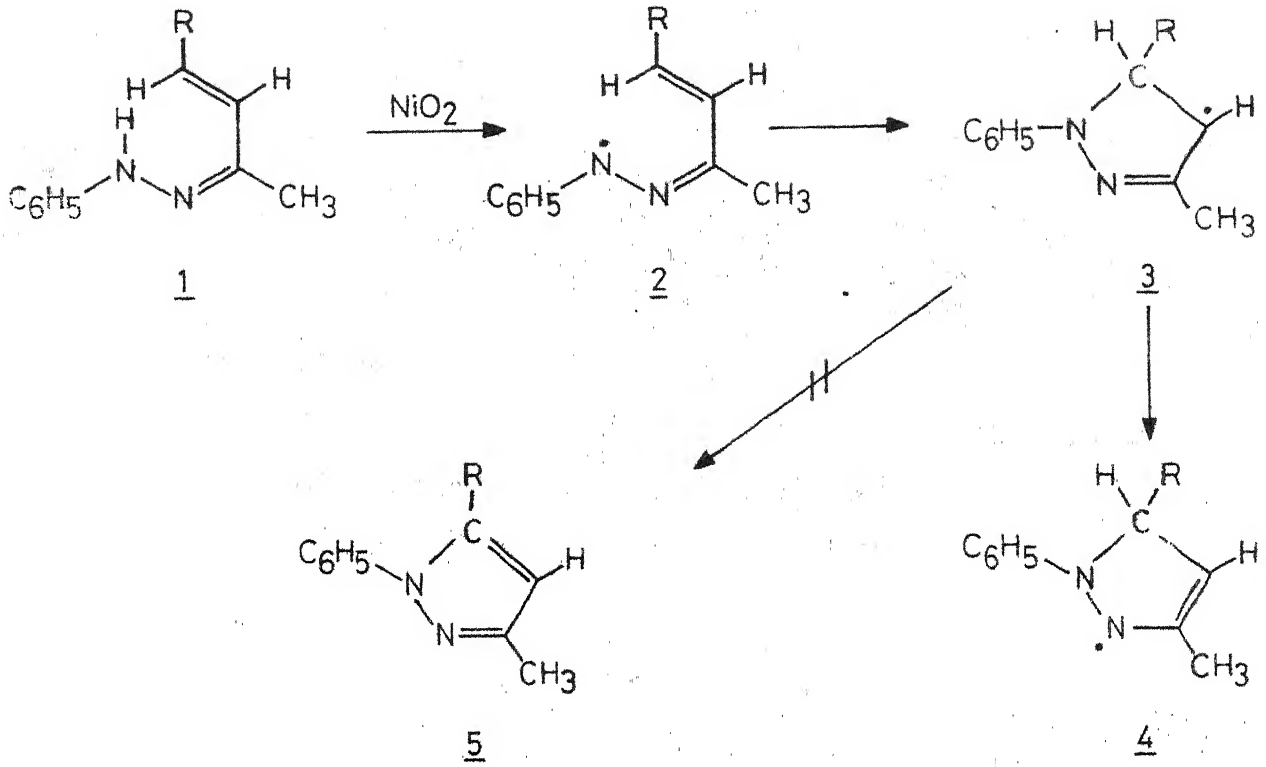
II. 2 RESULTS AND DISCUSSION

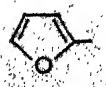
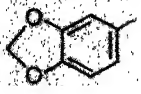
Several organic substrates such as aldehyde and ketone phenylhydrazones, chalcone phenylhydrazones and pyrazolines have been oxidized using different non-stoichiometric oxides such as manganese dioxide[2-4] and nickel peroxide.[5]

Benzophenone phenylhydrazone, for example, on oxidation with manganese dioxide gives a mixture of benzophenone and biphenyl. Under similar conditions, aldehyde phenylhydrazones give a mixture of several oxidative dimers, triazoles and biphenyl.[2] Chalcone phenylhydrazones give rise to pyrazoles when oxidized with manganese dioxide in benzene solution.[3] Under similar conditions, pyrazolines give excellent yields of pyrazoles.[3] The object of the present investigation had been to study the oxidation of few benzylideneacetone phenylhydrazones using nickel peroxide to examine the nature of the products formed in these oxidations.

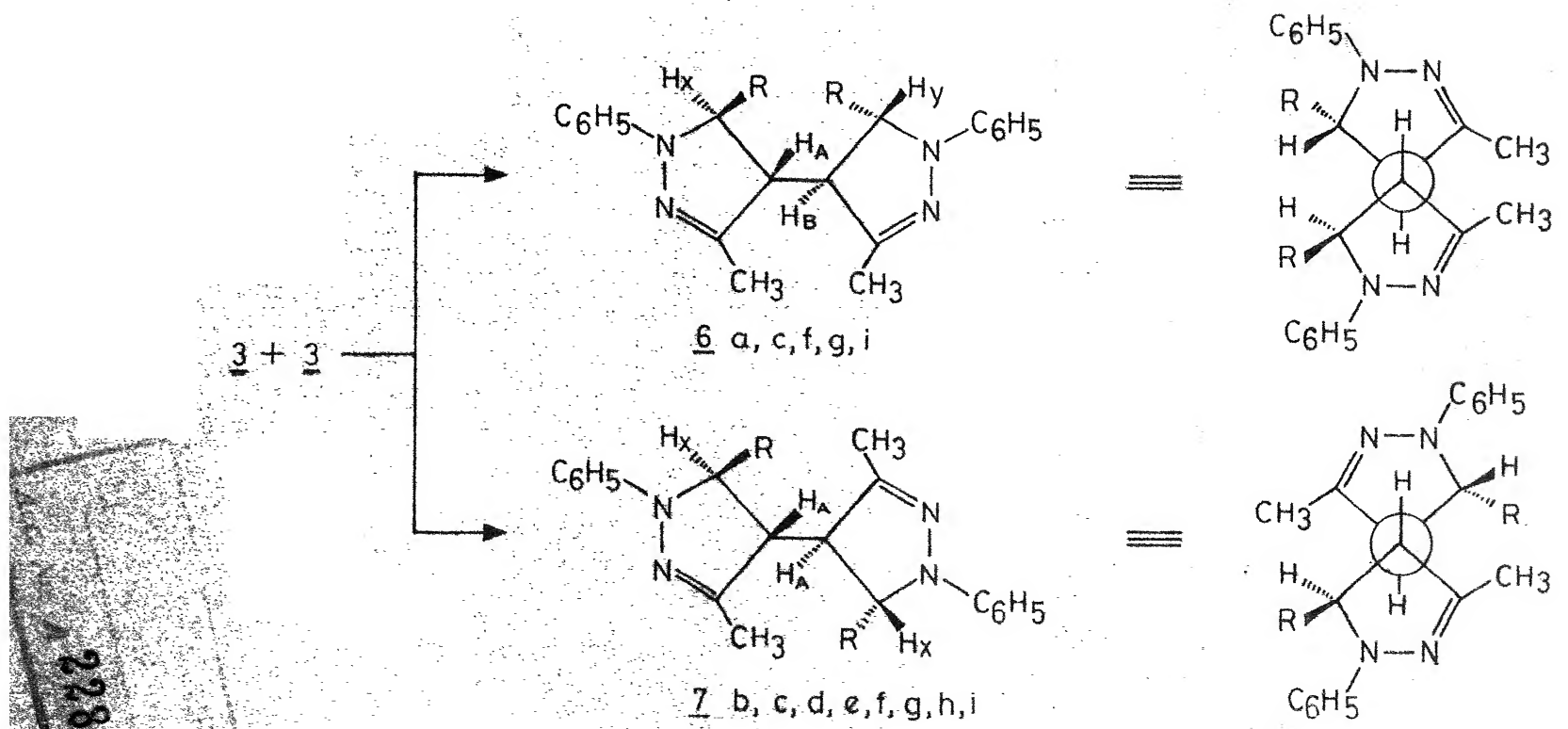
Treatment of benzylideneacetone phenylhydrazone (1a) with nickel peroxide in benzene solution at room temperature gives a product, melting at 310°, identified as an oxidative dimer of 1a, which analyses for $C_{32}H_{30}N_4$ (Mol. wt. 470, mass spectrometry). Of the four different possible structures, 6a, 7, 8 and 9 for the oxidative dimer of 1a, we have assigned 6a, representing the dl-form of 1,1',5,5'-tetraphenyl-3,3'-dimethyl-4,4'-bipyrazoline for our compound, on the basis of spectral evidences (Scheme II.1). The uv spectrum of 6a shows an absorption maximum at 289 nm with

Scheme II·1

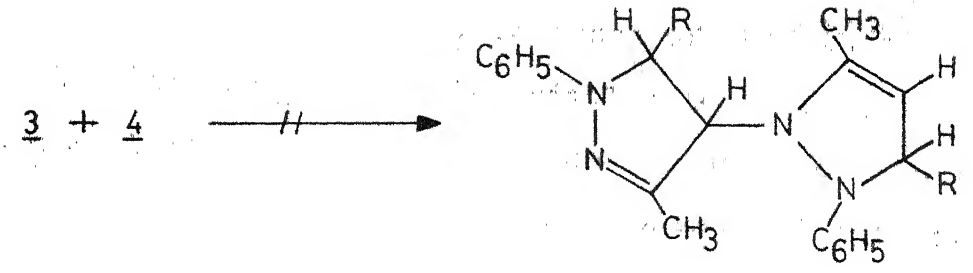


a, R = C_6H_5
b, R = o - $CH_3C_6H_4$
c, R = m - $CH_3C_6H_4$
d, R = p - $CH_3C_6H_4$
e, R = o - ClC_6H_4
f, R = m - ClC_6H_4
g, R = p - ClC_6H_4
h, R = 
i, R = 

Scheme II·1 (Contd.)



heme II·1 (Contd.)



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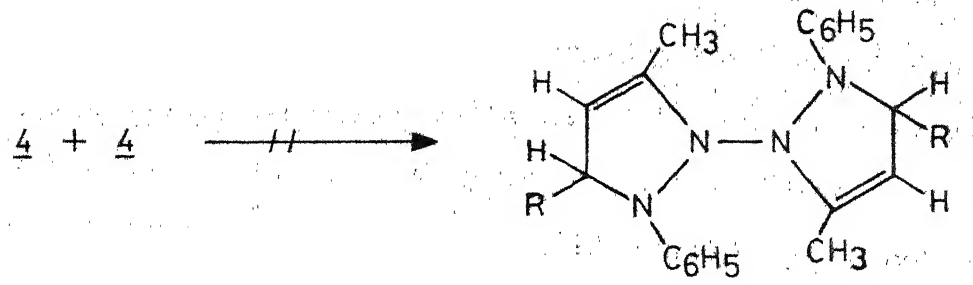


9

a high extinction coefficient (ϵ ,39,500), which is nearly twice the extinction coefficient for an analogous pyrazoline derivative such as 1,5-diphenyl- and 1-phenyl-3-methyl-Δ^2-pyrazolines.[6,7] The ir spectrum of 6a is also in agreement with that of 1,3,5-trisubstituted pyrazolines.[7,8] In addition, the oxidative dimer 6a gives a deep violet coloration, on treatment with a mixture of sodium nitrate and sulfuric acid, a test which is characteristic of 1-arylpyrazolines (Knorr pyrazoline test).[9]

It would be expected that the nmr spectral features of 6a are quite different from those of the other two oxidative dimers 8 and 9, but similar to that of structure 7 (Scheme II.1). Although the product that we obtain in the oxidation of 1a is quite insoluble in most of the common organic solvents, its nmr spectrum in trifluoroacetic acid clearly shows chemical shifts at 1.9 δ (6H), 4.09 δ (2H), 5.24 δ (2H) and 7.28 δ (20H) (Figure II.1). Of these, the signal at 1.9 δ has been assigned to the two methyl protons, whereas, the broad, poorly resolved multiplets at 4.09 δ and 5.24 δ are assigned to the tertiary protons at 4,4'-positions (A,B) and 5,5'-positions (X,Y), respectively. In the nmr spectrum of an analogous oxidative dimer from 3-methyl-benzylideneacetone phenylhydrazone (1c), however, the tertiary proton signals A and B appear as two distinct doublets centred around 2.89 δ (1H, J=2.6Hz, A or B) and 2.91 δ (1H, J=2.6Hz, A or B). Similarly, the tertiary protons, X and Y also show two distinct doublets centred around

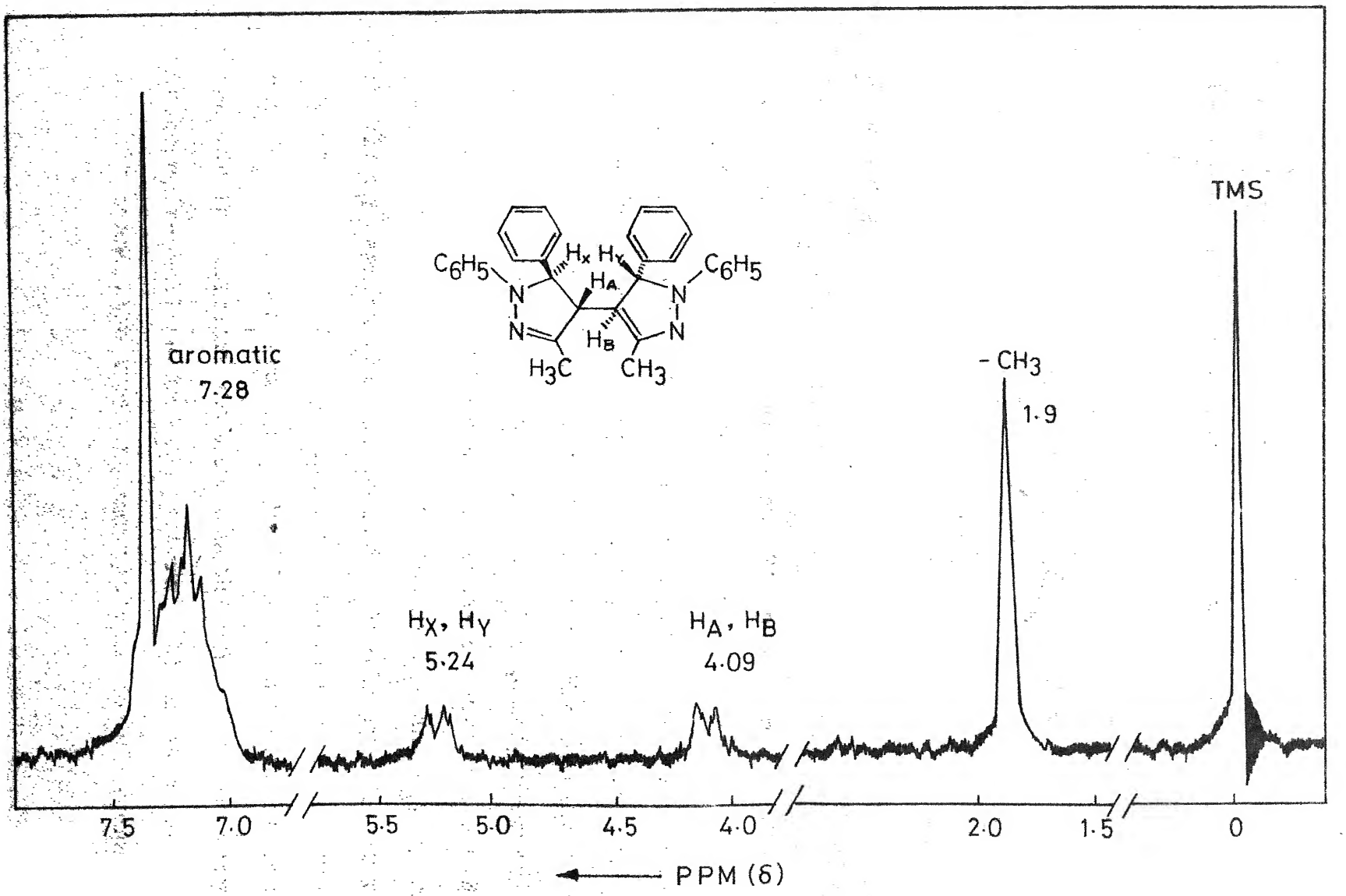
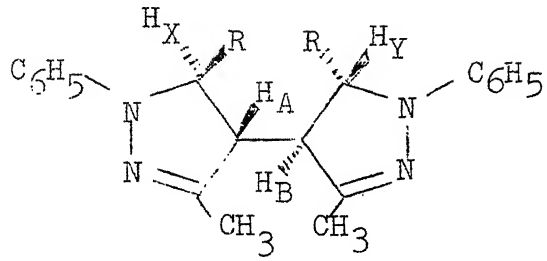


Fig.II.1 NMR spectrum (100MHz) of dl-1,1',5,5'-tetraphenyl-3,3'-dimethyl-4,4'-bipyrazoline (6a)

5.06 δ (1H, J=2.6Hz, X or Y) and 5.08 δ (1H, J=2.6Hz, X or Y). In addition, the spectrum of 6c shows a singlet at 2.16 δ (6H)



6a R = C_6H_5

6c R = m-$CH_3C_6H_4$

due to methyl protons at 3- and 3'- positions, another singlet at 2.27 δ (6H) due to m-methyl protons of the phenyl-ring at 5- and 5'- positions and a multiplet centred around 6.7 δ (18H) corresponding to the aromatic protons (Figure II.2).

The nmr spectral features of the oxidative dimer are not in the agreement with the N-N coupling product 9. Molecular models of 9 show free rotation across the N-N bond and hence the tertiary protons at C_3- and $C_{3'}$- positions should be magnetically equivalent. Similarly, the vinylic protons at C_4- and $C_{4'}$- positions should also be equivalent and hence the spectrum of 9 should show two sets of doublets, one for the tertiary protons and the other for the vinylic protons, resembling an A_2X_2 pattern. It might be mentioned in this connection that the nmr spectrum of a compound such

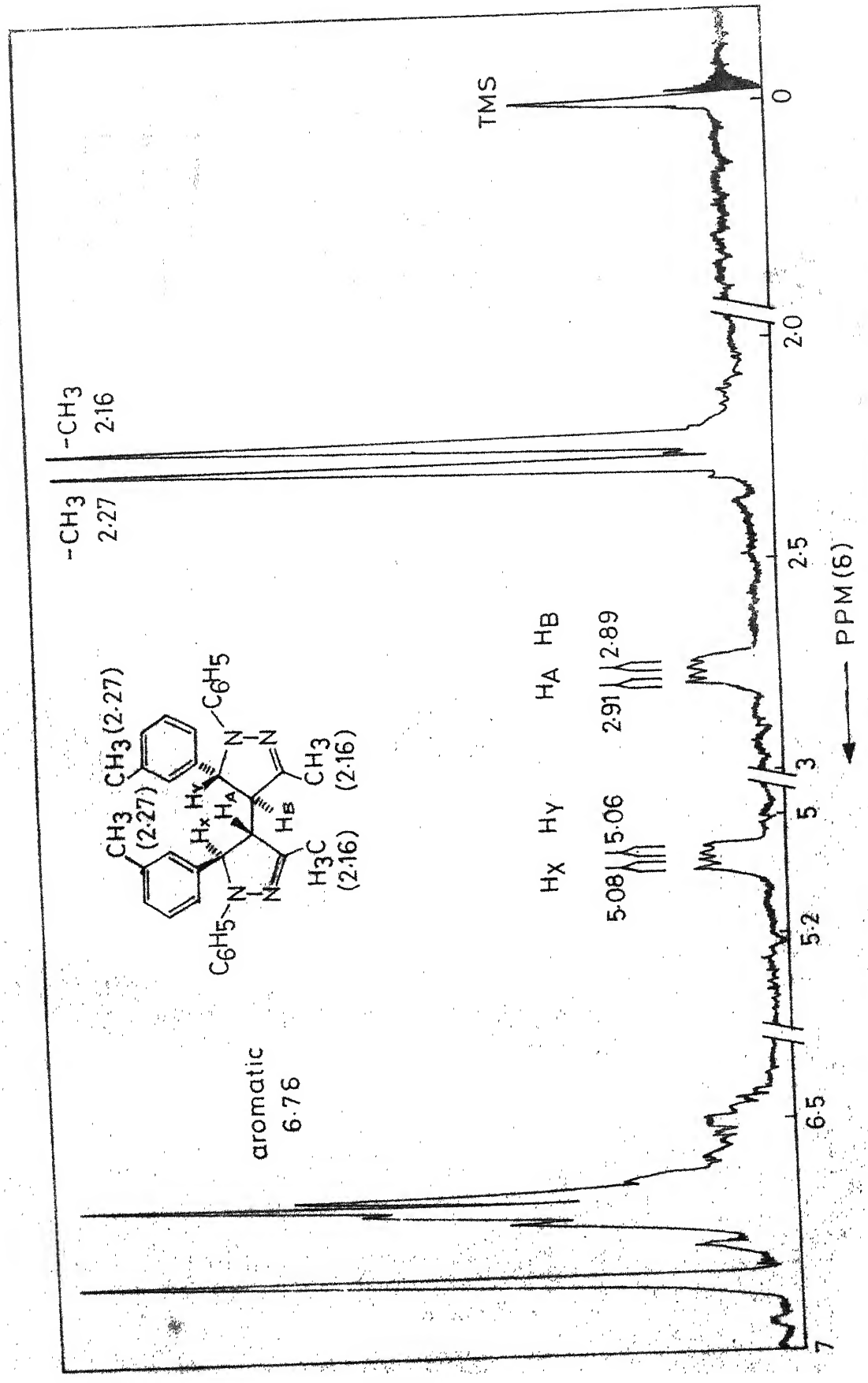
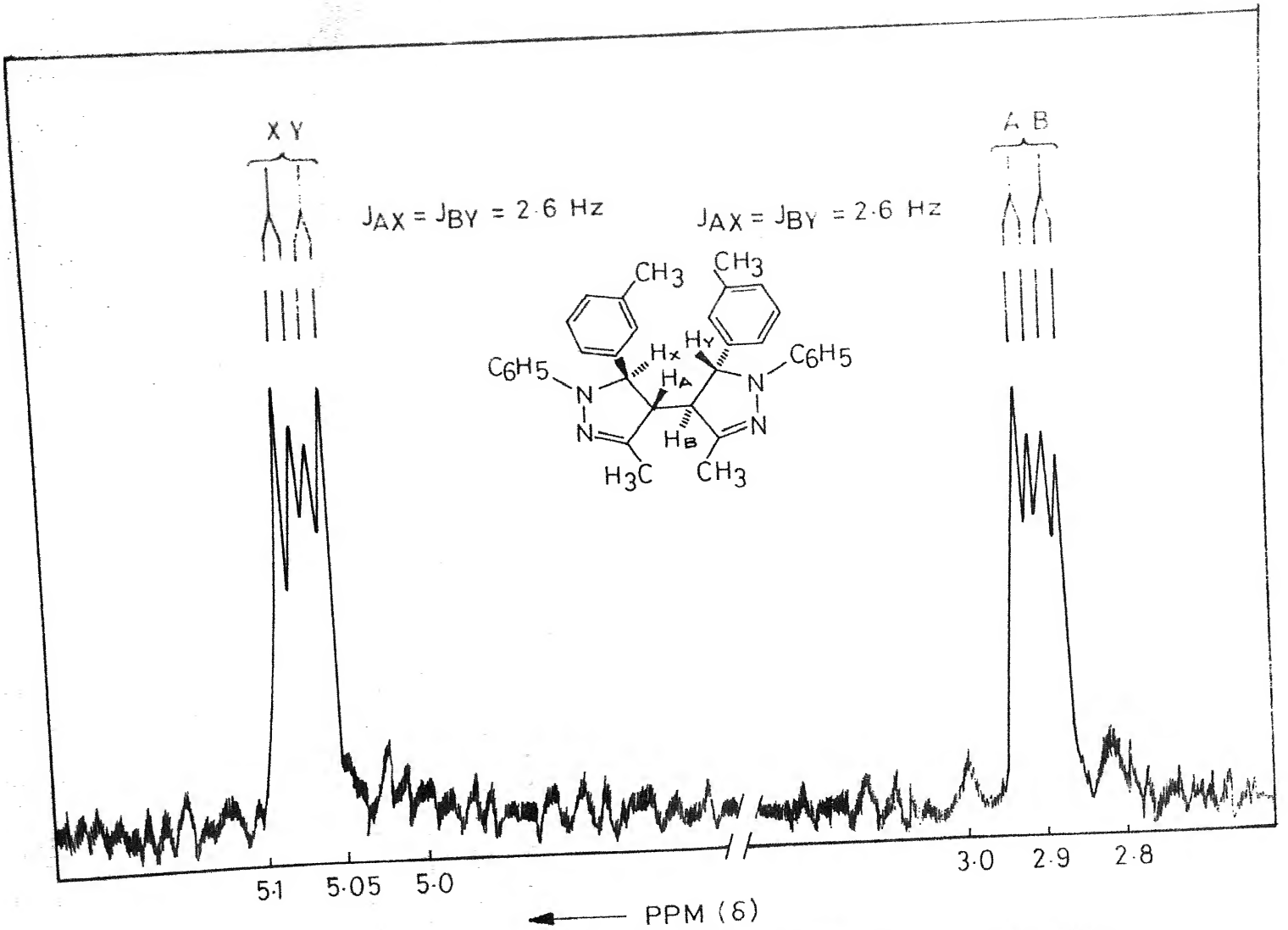
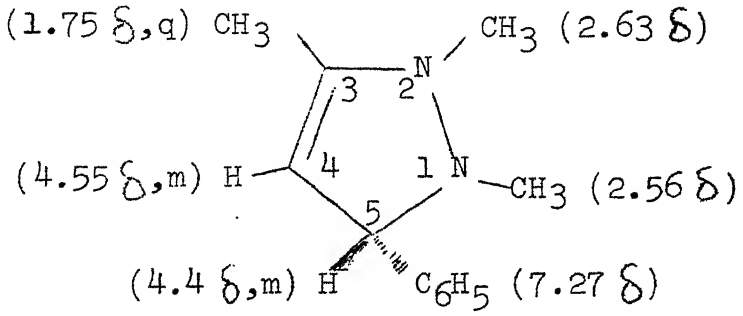


Fig.II.2 NMR spectrum (100MHz) of dl-1,1'-diphenyl-3,3'-dimethyl-5,5'-di-(m-tolyl)-4,4'-bipyrazoline (6c)



NMR spectrum (100MHz) of dl-1,1'-diphenyl-3,3'-dimethyl 5,5'-di-(m-tolyl)-4,4'-bipyrazoline (6e) (expanded)

as 1,2,3-trimethyl-5-phenyl- Δ^3-pyrazoline, which is structurally similar to the pyrazoline fragments in 9, shows a quartet for the C_3- methyl group. The vinylic proton and the tertiary proton at C_5- appear as multiplets.[10] The appearance of the vinylic proton at C_4- and the tertiary proton at C_5- as



multiplets, is attributed to the CH_3 protons at C_3- position. If structure 9 were to represent the oxidative dimer, one would expect a spectrum similar to that of 1,2,3-trimethyl-5-phenyl- Δ^3-pyrazoline. On similar grounds, we would expect the nmr spectrum of 8 to be quite different from the experimentally observed spectrum. The structure for the oxidative dimer of 1c has, therefore, to be represented by either 6c or 7c.

The nmr spectra of pyrazolines have been examined by several workers and it has been shown that the trans-coupling constant in 4,5-disubstituted pyrazolines can vary anywhere between 1.5 - 9.0 Hz.[11-13] Also, it has been observed that J_{trans} decreases with increasing polarity of the

substituent at 4- position. Since the coupling constant for the two tertiary protons A and X is of the order of 2.6 Hz, these should be trans with respect to each other. With a view to deciding between the structures 6c and 7c for the oxidative dimer of 1c, we have examined their models and found that there is hindrance to free rotation in these molecules due to the methyl groups at both 3- and 3'- positions. Further, it is observed that the most favourable conformation for 6c is one in which the two protons A and B are trans to each other with a dihedral angle ranging between 80-100°. The appearance of four distinct doublets for the tertiary protons (A and B as well as for X and Y) can be rationalised in terms of the magnetic non-equivalence of A and B, resulting in the coupling of A with X and B with Y, respectively and vice-versa ($J_{Ax} = J_{By} = 2.6$ Hz). The absence of any appreciable coupling between the two protons A and B may be due to the fact that the dihedral angle between them is around 90°. In the case of 7c, the hindrance to free rotation across the C_4-$C_{4'}$ bond is not appreciable and hence both groups of protons A and B as well as X and Y become magnetically equivalent. Accordingly, one would expect two sets of doublets in the nmr spectrum, similar to an A_2X_2 pattern. Thus, on the basis of nmr spectral evidences, we would rule out structure 7c and favour 6c for the oxidative dimer of 1c. Additional support for the structure 6c comes from a theoretical analysis of the spectrum as an ABXY pattern

an N-N coupling occurs, then the 1,1'-bipyrazoline derivative 8, would be expected; a C-N coupling, on the other hand, would lead to the formation of bipyrazoline 9 (Scheme II.1). In the oxidation of benzylideneacetone phenylhydrazone (1a), we could isolate only the C-C coupling product 6a.

With a view to testing the generality of the oxidation of benzylideneacetone phenylhydrazones for the preparation of bipyrazoline derivatives, we have examined the oxidations of few representative benzylideneacetone phenylhydrazones. Thus, treatment of 2-methylbenzylideneacetone phenylhydrazone (1b) with nickel peroxide, in benzene solution at room temperature, gives 30% yield of a product, identified as meso-1,1'-diphenyl-3,3'-dimethyl-5,5'-di-(o-tolyl)-4,4'-bipyrazoline (7b). The sturcture of 7b is confirmed on the basis of analytical results and spectral data. The nmr spectrum of 7b shows two sharp singlets at 2.1 δ (6H) and 2.26 δ (6H) due to the methyl groups at the 3-position of the pyrazoline nucleus and the o-methyl protons, respectively. In addition, the spectrum shows two doublets at 2.45 δ (2H, J=1Hz) and 5.57 δ (2H, J=1Hz) due to tertiary protons at 4,4'- positions and the benzylic protons, respectively, resembling an A_2X_2 pattern. The aromatic protons appear as a multiplet centred around 7.07 δ (18H). (Figure II.3). It is observed from the molecular model of 7b, that there is a slight hindrance to free rotation around the C_4-C_4' bond. Since the molecule is symmetric, the two

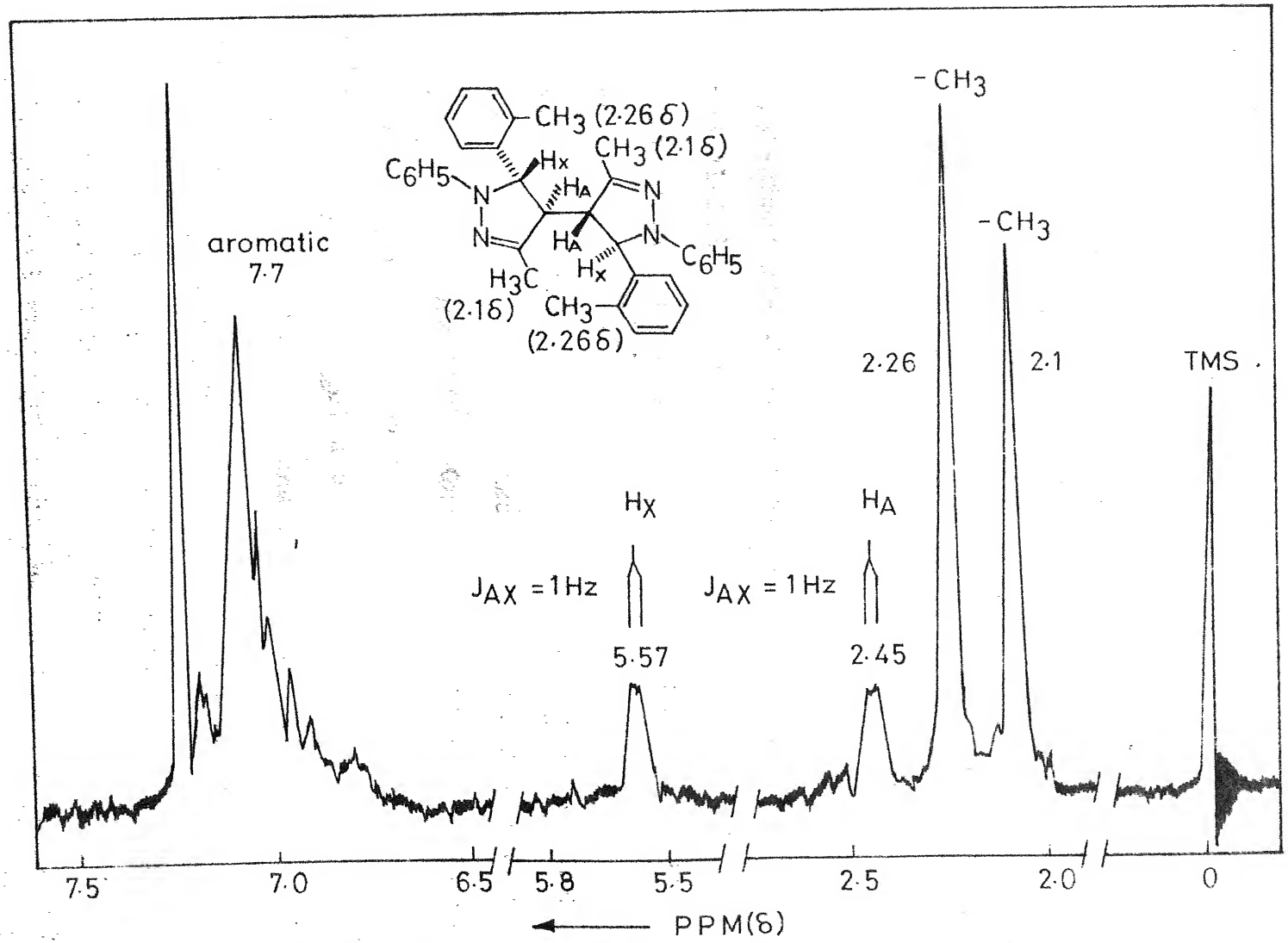


Fig.II.3 NMR spectrum (60MHz) of meso-1,1'-diphenyl-3,3'-dimethyl-5,5'-di-(o-tolyl)-4,4'-bipyrazoline (7b)

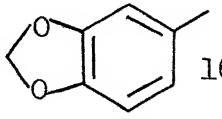
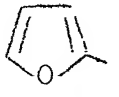
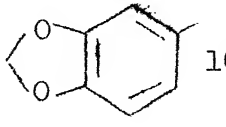
tertiary protons become magnetically equivalent. Similarly, the benzylic protons would also become magnetically equivalent. The small coupling constant between the tertiary proton and the benzylic protons is attributed to the substituents at C_4- and $C_{4'}$- positions. A probable route to the formation of 7b is shown in Scheme II.1.

The oxidation of 2-methylbenzylideneacetone phenylhydrazone (1b) with nickel peroxide gives 30% yield of meso-1,1'-diphenyl-3,3'-dimethyl-5,5'-di-(o-tolyl)-4,4'-bipyrazoline (7b), whereas, 3-methylbenzylideneacetone phenylhydrazone (1c) gives a mixture of both meso-1,1'-diphenyl-3,3'-dimethyl-5,5'-di-(m-tolyl)-4,4'-bipyrazoline (7c, 20%) and dl-1,1'-diphenyl-3,3'-dimethyl-5,5'-di-(m-tolyl)-4,4'-bipyrazoline (6c, 8%). Similarly, mixtures of both meso- and dl- forms of 4,4'-bipyrazolines are formed from 3-chlorobenzylideneacetone phenylhydrazone (1f), 4-chlorobenzylideneacetone phenylhydrazone (1g) and piperonylideneacetone phenylhydrazone (1i). On the other hand, 4-methylbenzylideneacetone phenylhydrazone (1d), 2-chlorobenzylideneacetone phenylhydrazone (1e) and furfurylideneacetone phenylhydrazone (1h) give exclusively the meso- forms of 4,4'-bipyrazoline.

II.3 INFRARED SPECTRA OF 4,4'-BIPYRAZOLINES

In the course of the present investigation, we have examined the infrared spectra of few 4,4'-bipyrazolines. The 4,4'-bipyrazolines that we have prepared (6 and 7) show several characteristic absorption bands in the region 4000-700 cm^{-1} and Table II.1 summarizes these data. It has

Infra-red Spectral Characteristics of 4,4'-Bipyrazolines

4,4'-Bi-pyrazoline	R	C=N	Skeletal vibrations of phenyl rings		C_6H_5-N	CH-N	Substituted benzene C-H out-of-plane bending
6a	C_6H_5	1595(vs)	1495(vs)	1450(vs)	1320(m)	1140(s)	750(s)
6c	m-$CH_3C_6H_4$	1600(vs)	1495(vs)	1450(m)	1330(m)	1130(m)	785(s), 765(s)
6f	m-ClC_6H_4	1590(vs)	1485(vs)	1420(s)	1330(m)	1120(m)	780(s), 750(s), 700(s)
6g	p-ClC_6H_4	1590(vs)	1480(s)	1425(s)	1330(m)	1120(m)	790(s), 735(s)
6i		1600(vs)	1490(vs)	1430(s)	1325(w)	1130(w)	815(s)
7b	o-$CH_3C_6H_4$	1590(vs)	1485(s)	1450(w)	1315(s)	1140(s)	750(s), 745(s)
7c	m-$CH_3C_6H_4$	1600(vs)	1495(s)	1430(w)	1300(m)	1135(s)	790(m), 765(s), 715(m)
7d	p-$CH_3C_6H_4$	1595(vs)	1495(s)	1430(m)	1320(m)	1140(s)	750(s), 720(s)
7e	o-ClC_6H_4	1585(vs)	1490(s)	1425(w)	1325(m)	1150(s)	760(s), 730(m)
7f	m-ClC_6H_4	1585(vs)	1485(s)	1410(m)	1300(m)	1140(s)	785(s), 745(s), 715(s)
7g	p-ClC_6H_4	1585(vs)	1480(s)	1425(m)	1305(m)	1140(s)	740(s), 720(m)
7h		1600(vs)	1495(s)	1430(w)	1305(m)	1135(m)	780(w), 770(w)
7i		1600(vs)	1500(s)	1440(m)	1340(m)	1150(s)	740(s)

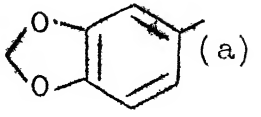
been observed that the spectral features of 4,4'-bipyrazolines are quite similar to those of 1,3,5-trisubstituted-Δ^2-pyrazolines.[7,8] The most interesting portion of the spectrum is in the range of 1400-1600 cm^{-1}, where one would expect absorption bands due to the C=N, as well as the usual C=C (aromatic) stretching vibrations. Thus, both the dl- and meso- isomers show a strong absorption band due to the C=N group around 1600 cm^{-1}; the phenyl skeletal vibrations are found between 1425-1450 cm^{-1}. In addition, absorption bands due to C_6H_5-N and CH-N vibrations are observed around 1300 and 1120 cm^{-1}, respectively. Strong absorption bands due to C-H out-of-plane bending vibrations are also seen in the region, 700-800 cm^{-1}.

II.4 NMR SPECTRA OF 4,4'-BIPYRAZOLINES

The nmr spectra of 4,4'-bipyrazolines are of interest. The proton positions in various dl-4,4'-bipyrazolines (6a,c,f,g,i), have been summarized in Table II.2. The nmr spectra of two representative dl-,4,4'-bipyrazolines namely, those of 1,1',5,5'-tetraphenyl-3,3-dimethyl-4,4'-bipyrazoline (6a) and 1,1'-diphenyl-3,3'-dimethyl-5,5'-di-(m-tolyl)-4,4'-bipyrazoline (6c) are shown in Figures II.1 and II.2, respectively. The spectra of dl- forms of 4,4'-bipyrazolines are characterized by the presence of a sharp singlet in the range of 1.8-2.3 δ, due to the methyl groups in the 3- and 3'- positions. The tertiary protons at 4- and 4'- positions appear as two doublets in the region 2.9-3.0 δ, as a result of the coupling of these protons

Table II.2

NMR Spectra of dl-4,4'-Bipyrazolines

Compound	R	CH_3 protons (in δ)	CH_3 attached to phenyl ring (in δ)	A or A' (in δ)	A or A' (in δ)	X or X' (in δ)	X or X' (in δ)	J_{AX} Hz.	$J_{A'X'}$ Hz.	Aromatic (in δ)
6a	C_6H_5 [a]	1.9(s)	-	4.09; poorly resolved		5.24; poorly resolved		-	-	7.28(m)
6c	m-$CH_3C_6H_4$ [b]	2.16(s)	2.27	2.89(d)	2.91(d)	5.06(d)	5.08(d)	2.6	2.6	6.7(m)
6f	m-ClC_6H_5 [b]	2.3(s)	-	2.96(d)	3.05(d)	5.29(d)	5.29(d)	2.5	2.5	7.17(m)
6g	p-ClC_6H_4 [a]	1.73(s)	-	4.05(d)	4.17(d)	4.92(d)	5.08(d)	2.5	2.5	6.82(m)
6i*	 [a]	1.8(s)	-	4.02; poorly resolved		4.87; poorly resolved		-	-	6.7(m); 7.0(m)

a) In trifluoroacetic acid; b) In deuterochloroform; s) Singlet; d) Doublet; m) Multiplet

* The dioxymethylene protons in 6i appear as a singlet at 6.1 ppm (2H).

with those of 5- and 5'- protons, and with a coupling constant ($J_{4,5} = J_{4',5'}$) ranging between 2.3 to 2.6 Hz. The small coupling constant is as a result of the conformational restrictions due to the presence of the substituents at positions 4- and 5- and similar observations have been made in the case of 1,3,4,5-tetrasubstituted Δ^2-pyrazolines.[11-13] In trifluoroacetic acid, however, the position of the proton at C_4 gets shifted to the region between 4.0 and 4.1 δ. The benzylic protons at 5- and 5'- positions of these 4,4'-bipyrazolines also show a pair of doublets in the region 4.9-5.4 δ, with a coupling constant ranging from 2.3 to 2.6 Hz. The aromatic protons appear as a multiplet around 7.0 δ.

The nmr spectral details of a few meso-4,4'-bipyrazolines are listed in Table II.3. The nmr spectra of two representative bipyrazolines, namely, those of meso-1,1'-diphenyl-3,3'-dimethyl-5,5'-di-(o-tolyl)-4,4'-bipyrazoline (7b) and meso-1,1'-diphenyl-3,3'-dimethyl-5,5'-di-(m-tolyl)-4,4'-bipyrazoline (7c) are shown in Figures II.3 and II.4, respectively. In all the meso-4,4'-bipyrazolines, the methyl protons at 3- and 3'-positions appear as sharp singlets in the region 1.95-2.1 δ. The tertiary protons at 4- and 4'- positions, as well as the benzylic protons at 5- and 5'- positions, appear as two doublets, in the region 2.5-3.0 δ and 5.4-5.9 δ, respectively, and with a coupling constant ($J_{4,5}$) in the range 1.0 to 1.5 Hz (A_2X_2 pattern The aromatic protons appear as a multiplet around 7.0 δ.

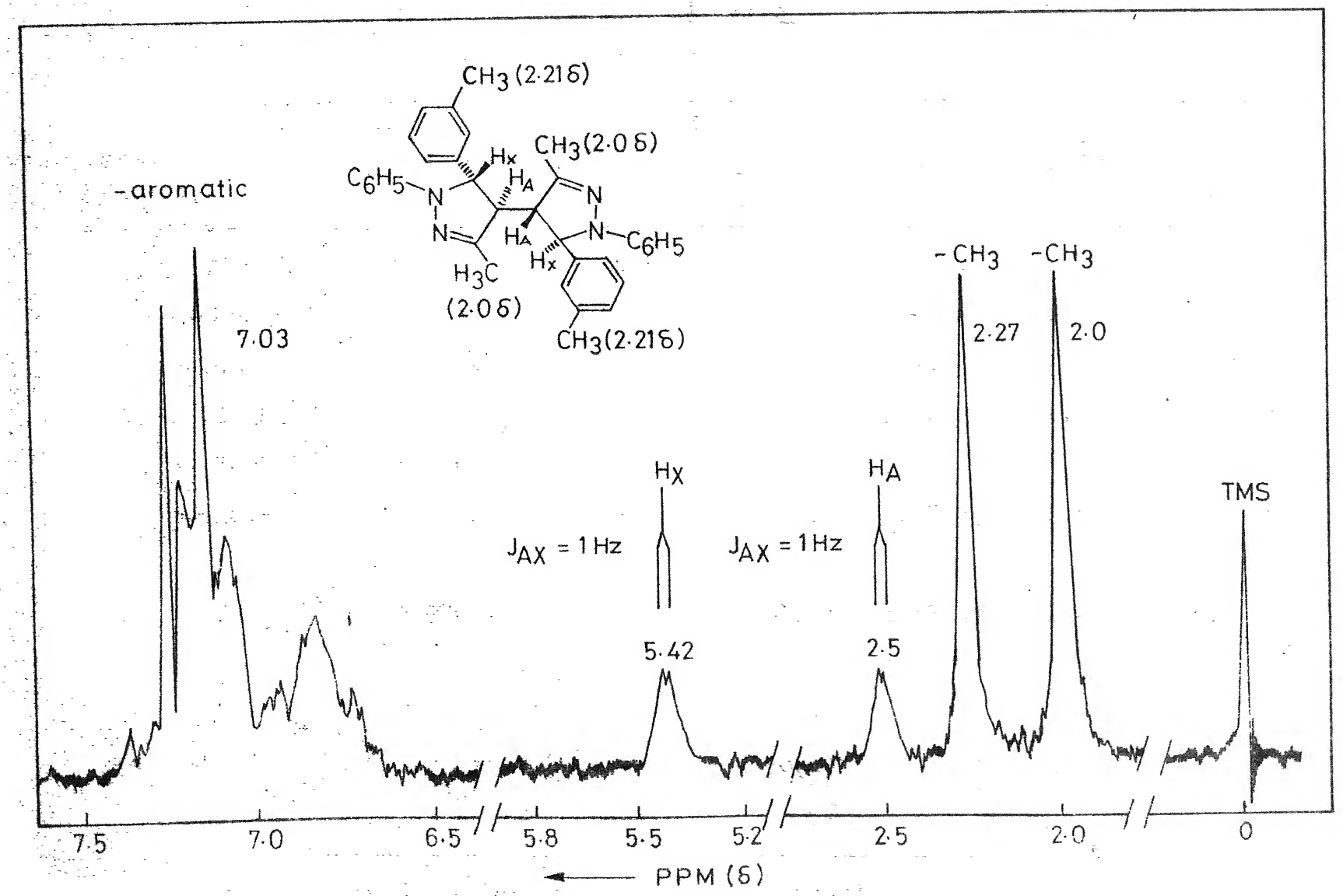
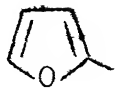
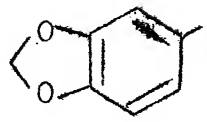


Fig.II.4 NMR spectrum (60MHz) of meso-1,1'-diphenyl-3,3'-dimethyl-5,5'-di-(m-tolyl)4,4'-bipyrazoline (7c)

Table II.3

NMR Spectra of meso-4,4'-Bipyrazolines

Compound	R	CH_3 protons (in δ)	CH_3 attached to phenyl ring (in δ)	A (in δ)	X (in δ)	J_{AX} (Hz.)	Aromatic protons (in δ)
7b	o-$CH_3C_6H_4$ (a)	2.1(s)	2.26(s)	2.45(d)	5.57(d)	1.0	7.07(m)
7c	m-$CH_3C_6H_4$ (a)	2.0(s)	2.27(s)	2.5(d)	5.42(d)	1.0	7.03(m)
7d	p-$CH_3C_6H_4$ (a)	1.95(s)	2.27(s)	2.43(d)	5.41(d)	1.0	7.05(m)
7e	o-ClC_6H_4 (a)	2.19(s)	-	2.83(d)	5.96(d)	1.0	7.26(m)
7f	m-ClC_6H_4 (a)	1.96(s)	-	2.43(d)	5.42(d)	1.5	7.07(m)
7g	p-ClC_6H_4 (a)	1.96(s)	-	2.40(d)	5.42(d)	1.5	7.04(m)
7h	 (a)	1.97(s)	-	2.91(d)	5.53(d)	1.0	6.22(m), 6.3(m), 7.25(m)
7i*	 (b)	2.03(s)	-	2.56(d)	5.48(d)	1.5	6.7(m)

a) In $CDCl_3$; b) In CD_3COCD_3, s) Singlet, d) Doublet, m) Multiplet

* The dioxymethylene protons in 7i appear as a singlet at 6.02 δ(2H).

II.5 MASS SPECTRAL FRAGMENTATION OF 4,4'-BIPYRAZOLINES

During the course of the present work, we have carried out a preliminary study concerning the mass spectral fragmentation of a few 4,4'-bipyrazolines. It has been observed that the mass spectral fragmentation of both the meso- and the dl- forms of 4,4'-bipyrazolines are identical in almost all details except in the relative intensities of few peaks. Figures II.5, II.6 and II.7 show the mass spectral fragmentation of a few representative 4,4'-bipyrazolines, namely dl- 1,1',5,5'-tetraphenyl-3,3'-dimethyl-4,4'-bipyrazoline (6a), dl-1,1'-diphenyl-3,3'-dimethyl-5,5'-di-(p-chlorophenyl)-4,4'-bipyrazoline (6g) and meso-1,1'-diphenyl-3,3'-dimethyl-5,5'-di-(p-chlorophenyl)-4,4'-bipyrazoline (7g), respectively. The mass spectrum of 6a shows the molecular ion peak at m/e 470. In addition, several peaks at m/e 379, 289, 274, 247, 235, 171, 156, 144, 128, 115 and 77 are observed. A probable fragmentation mode for 6a is shown in Scheme II.2. The peak at m/e 379 has been assigned to the ion 6aa which may be formed by the loss of phenyl nitrene from the molecular ion. Such a loss of phenyl nitrene is well known in the photolytic and thermal decompositions, as well as under electron impact.[17-19] The peaks at m/e 289, 274 and 247 have been assigned to fragments 6ab, 6ac and 6ad respectively, formed by the loss of neutral molecules like Schiff's bases and HCN or radicals like methyl, and finally giving a stabilized ion, as shown in Scheme II.2. The peak at m/e 235 corresponds to half the molecular ion

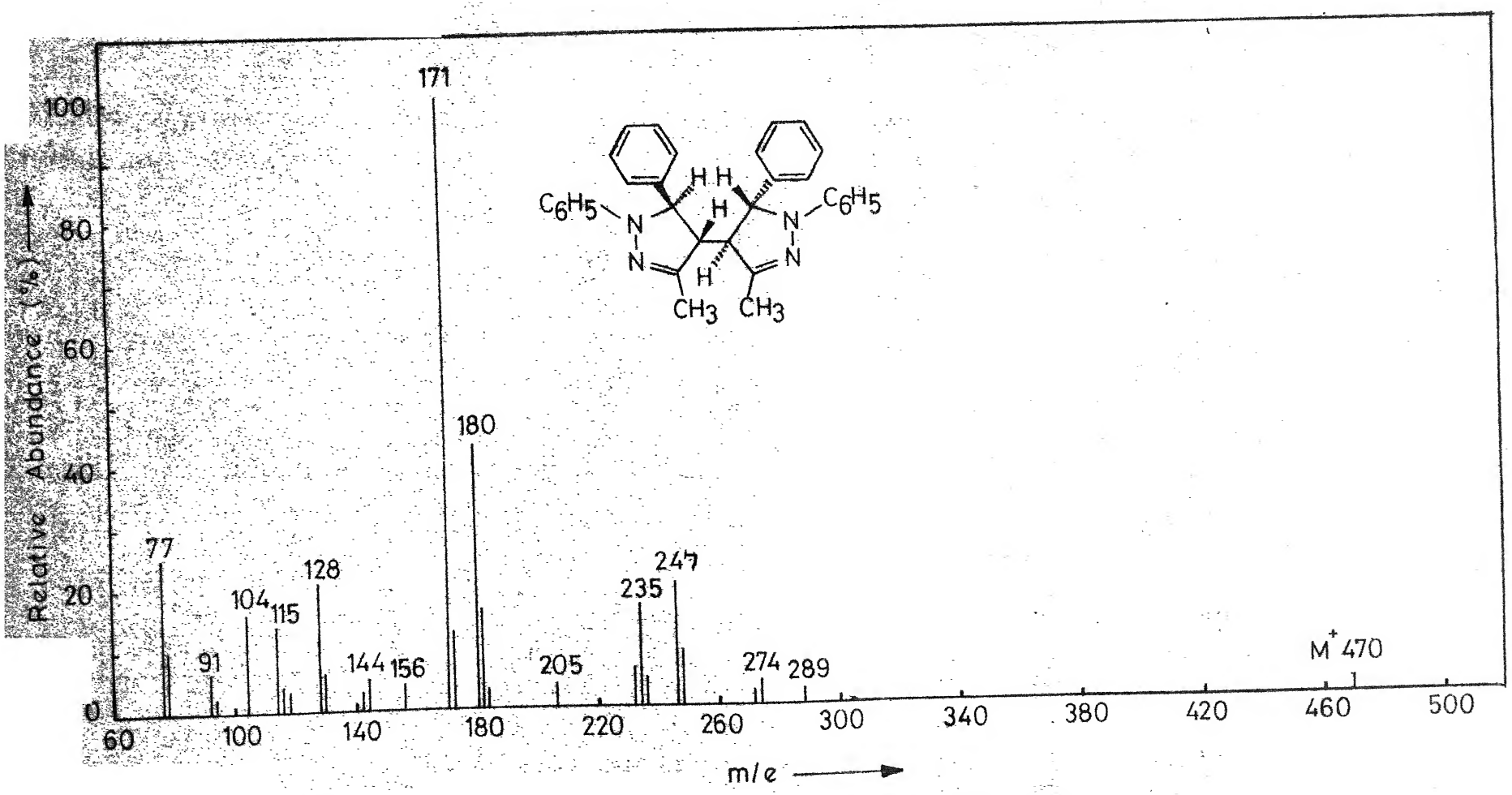


Fig.II.5 Mass spectrum of dl-1,1',5,5'-tetraphenyl-3,3'-dimethyl-4,4'-bipyrazoline (6a)

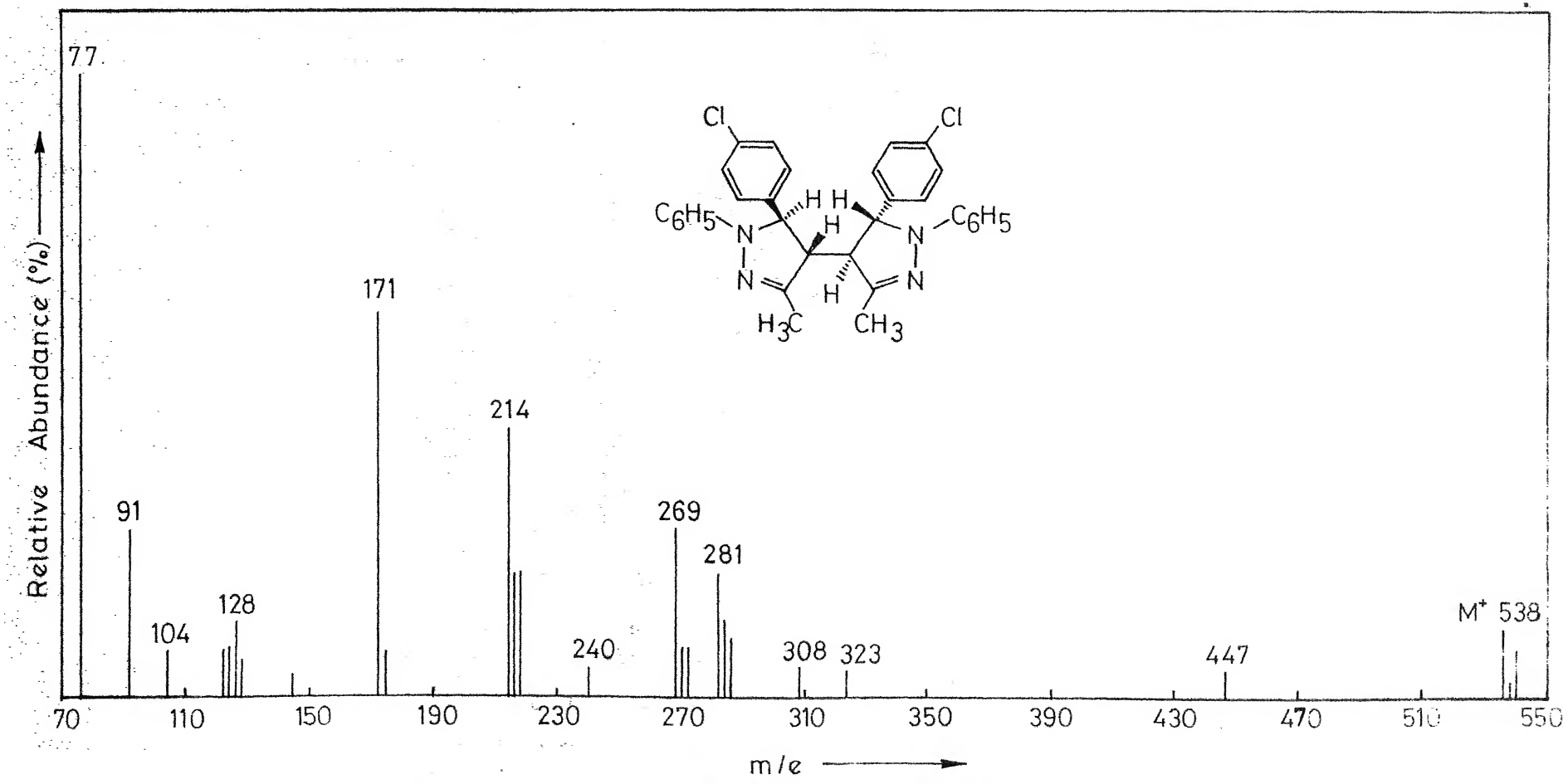


Fig.II.6. Mass spectrum of dl-1,1'-diphenyl-3,3'-dimethyl-5,5'-di-(p-chlorophenyl)-4,4'-bipyrazoline (6g)

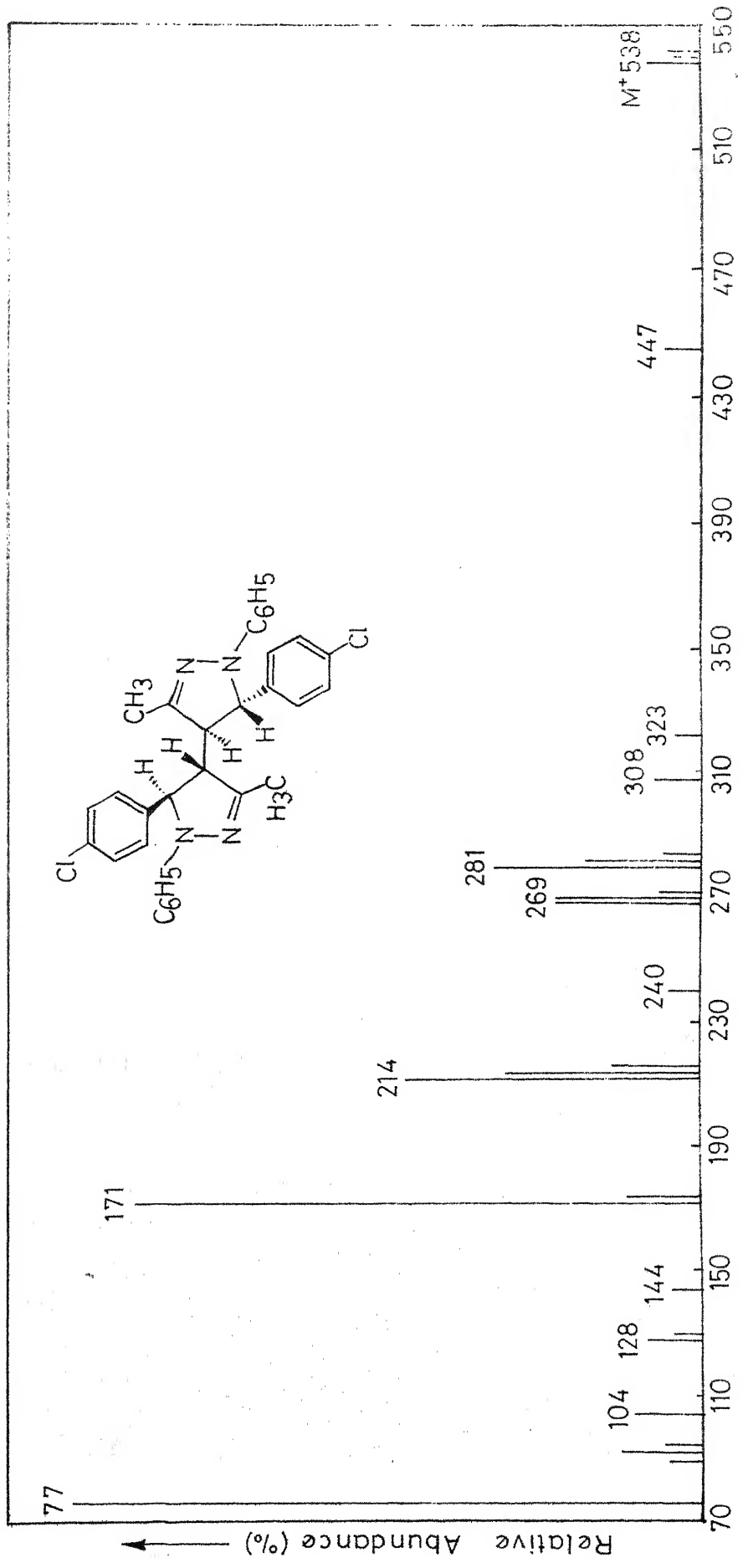
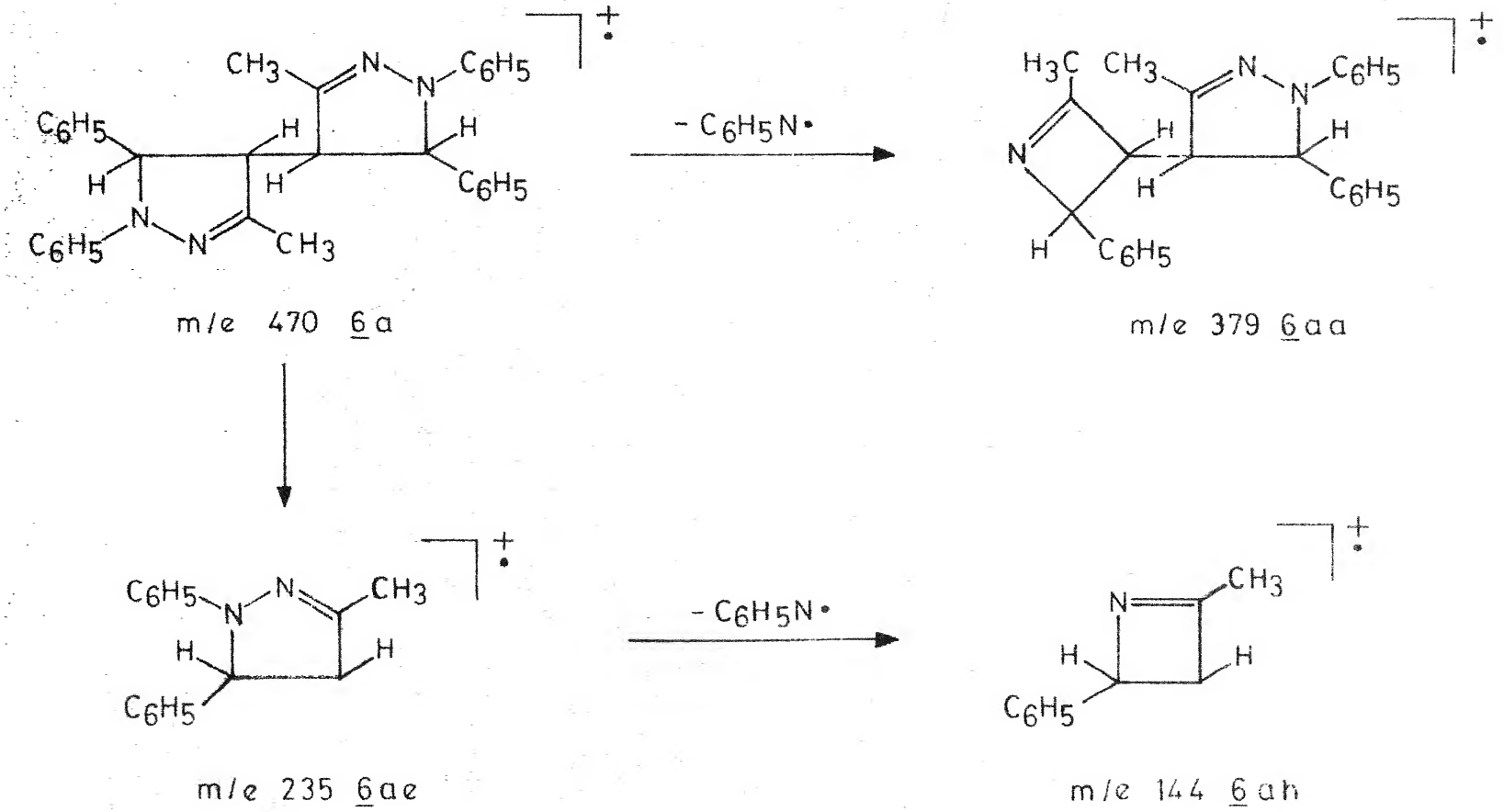
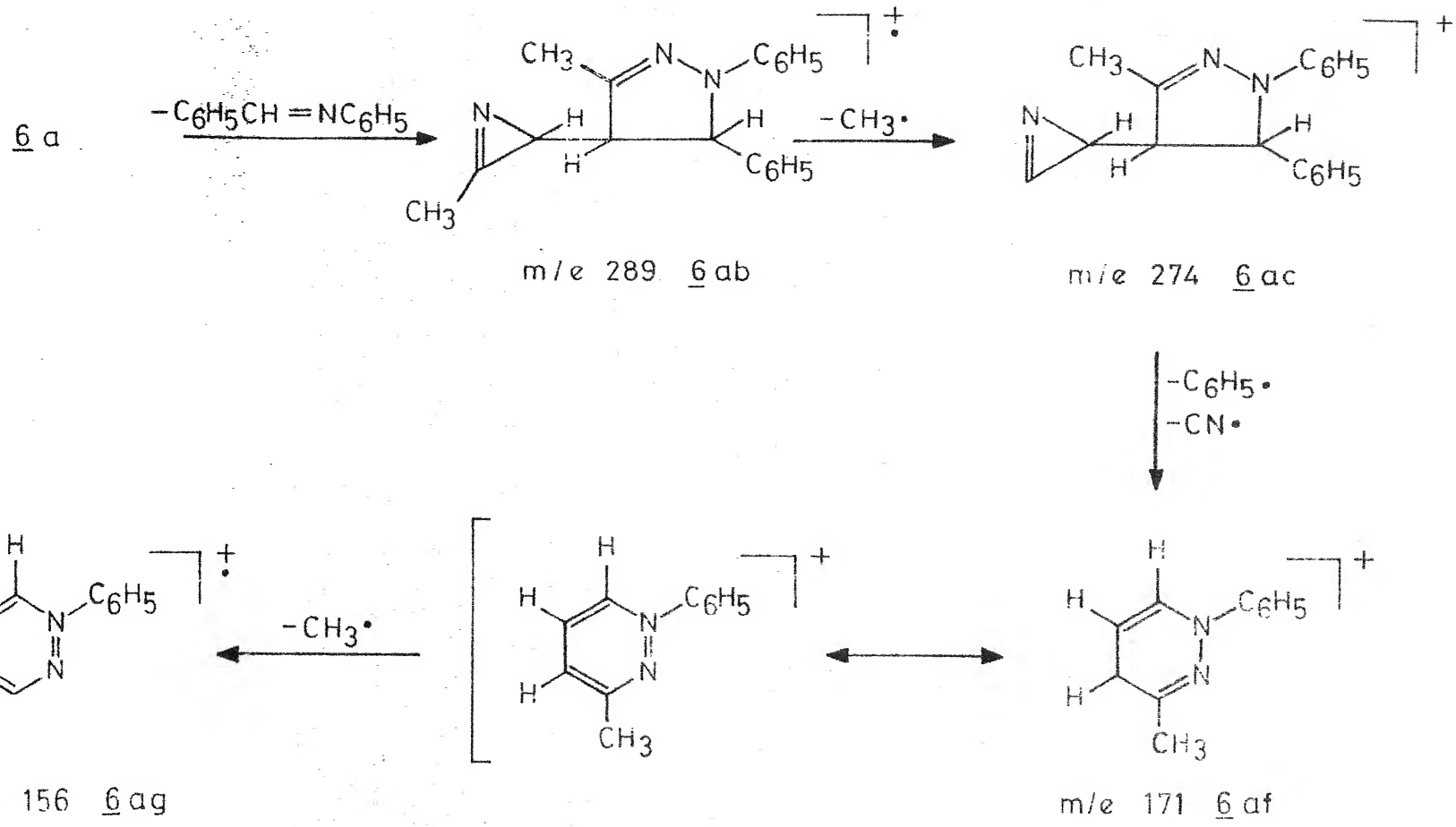


Fig.II.7 Mass spectrum of meso-1,1'-diphenyl-3,3'-dimethyl-5,5'-di-(p-chlorophenyl)-4,4'-bipyrazoline (7g)

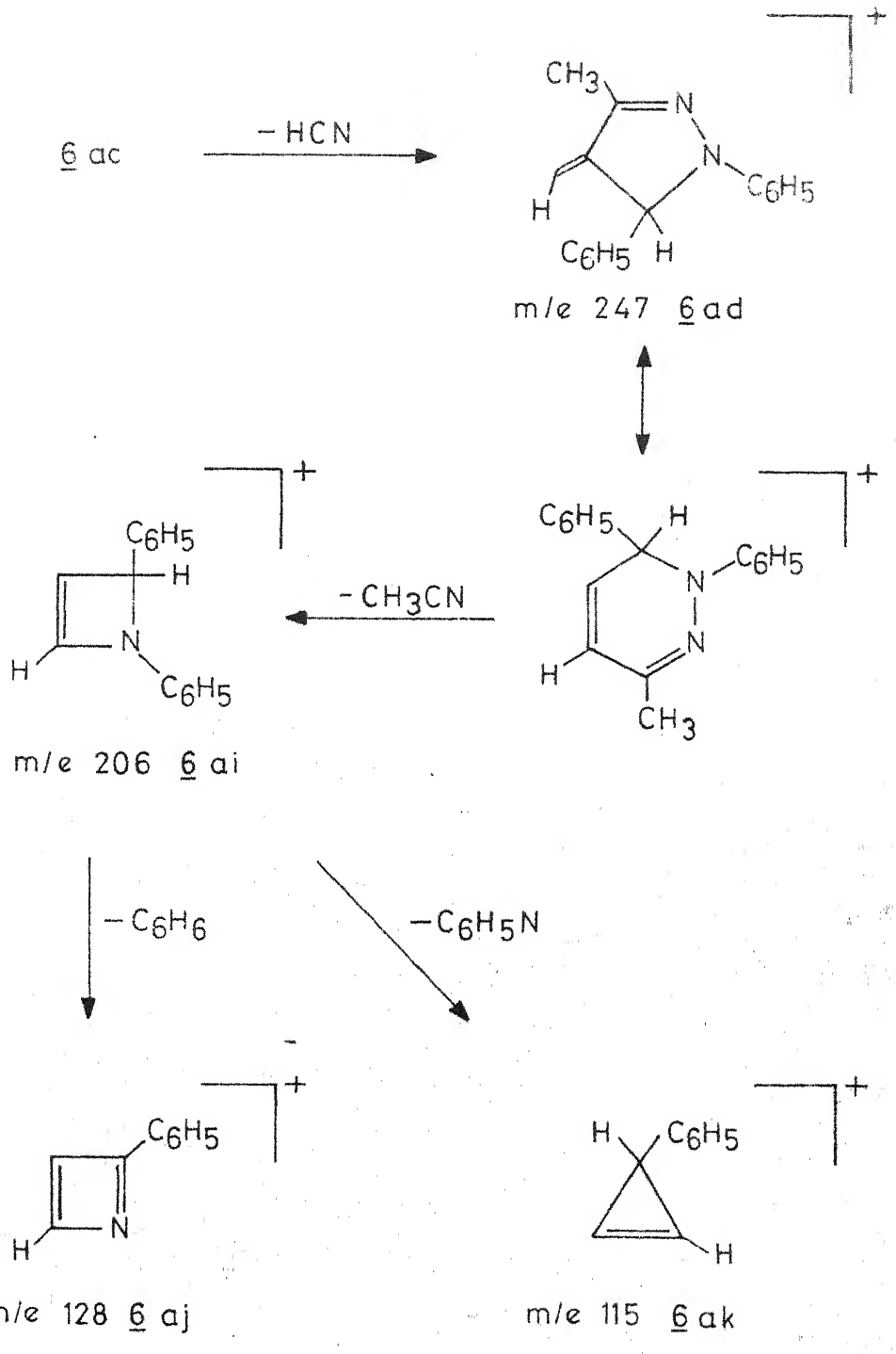
Scheme II·2



Scheme II·2 (Contd.)



Scheme II·2 (Contd.)



peak and is assigned to the pyrazoline ion 6ac. The fact that a peak at half the molecular ion peak is observed indicates that the molecule is symmetric across a single bond. It is interesting to note that in the mass spectra of all the 4,4'-bipyrazolines we could observe this $M/2^{+}$ ion. The most significant peak is seen at m/e 171 which is the base peak and is assigned the structure 6af. This might be due to the pyrazine ion formed from 6ac or 6ad by rearrangement and/or loss of some groups. This is a characteristic peak present in all 4,4'-bipyrazolines. Other peaks at 156 and 144 mass units could be due to fragments 6ag and 6ah, respectively. Similarly, the peaks at mass units 206, 128 and 115 could be due to fragments formed from 6ad.

II.6 EXPERIMENTAL

Starting Materials

Nickel peroxide (65 g) was prepared by the treatment of nickel sulfate (130 g) with a mixture of sodium hypochlorite (6% solution, 300 ml) and sodium hydroxide (42 g), as per a reported procedure.[20] The oxygen content of this sample was found to be of the order of 2.8×10^{-3} g-atom per gram of nickel peroxide. Benzylideneacetone phenylhydrazone,[21] mp 157°, 2-chlorobenzylideneacetone phenylhydrazone,[22] mp 92-93°, 4-chlorobenzylideneacetone phenylhydrazone,[23] mp 160°, 2-methylbenzylideneacetone phenylhydrazone,[24] mp 138°, 4-methylbenzylideneacetone phenylhydrazone,[24] mp 154°, furfurylideneacetone phenylhydrazone,[25] mp 131-32° and

piperonylideneacetone phenylhydrazone,[26] mp 163° were prepared from the corresponding benzylideneacetones and phenylhydrazine.

3-Methylbenzylideneacetone phenylhydrazone(6) was prepared by refluxing a mixture of 3-methylbenzylideneacetone (1.6 g, 10 mmol) and phenylhydrazine (1.08 g, 10 mmol) in ethanol. Removal of the solvent gave a product which was recrystallized from ethanol to give 2.2 g (80%) of 3-methylbenzylideneacetone phenylhydrazone, mp 135°.

Anal. Calcd for $C_{17}H_{18}N_2$: C, 81.60; H, 7.20; N, 11.20. Found: C, 81.68; H, 7.00; N, 11.60.

The ir spectrum (KBr) showed absorption bands at 3300 and 1608 cm^{-1} corresponding to N-H and C=N groups, respectively.

The uv spectrum (cyclohexane) was characterized by the following absorption maxima: 218 nm (ϵ ,14,900), 256 (15,000), 356 (28,700).

3-Chlorobenzylideneacetone phenylhydrazone (6f) was prepared by stirring a mixture of 3-chlorobenzylideneacetone (1.37 g, 7.5 mmol) phenylhydrazine (0.82 g, 7.5 mmol) and acetic acid (1 ml) in ethanol (3 ml) for 15 minutes. The solid which separated out was recrystallized from ethanol to give 1.25 g (63%) of 6f, mp 125-26°.

Anal. Calcd for $C_{16}H_{15}N_2Cl$: C, 70.98; H, 5.55; N, 10.35. Found: C, 70.87; H, 5.63; N, 10.19.

The ir spectrum (KBr) of 6f showed an N-H band at 3300 and C=N band at 1600 cm^{-1}.

The uv spectrum (cyclohexane) was characterized

by the following absorption maxima at 220 nm (ϵ ,16,000), 254 (15,000) and 350 (30,000).

Oxidation of Benzylideneacetone Phenylhydrazone (1a)

A In Benzene at Room Temperature

A mixture of benzylideneacetone phenylhydrazone (1a) (2 g, 8.4 mmol) and nickel peroxide (4 g) was stirred in benzene (200 ml) for 4 hr at room temperature. Removal of the inorganic material and of the solvent gave a red viscous liquid which on treatment with ethanol gave 1.4 g of a solid material. Recrystallization of this product from a mixture (1:1) of methylene chloride and ether gave 1.2 g (70%) of dl-1,1', 5,5'-tetraphenyl-3,3'-dimethyl-4,4'-bipyrazoline (6a), mp 310°.

Anal. Calcd for $C_{32}H_{30}N_4$: C, 81.70; H, 6.38; N, 11.91; Mol. wt., 470. Found: C, 81.68; H, 6.54; N, 12.02; Mol. wt.,470 (mass spectrometry).

The uv spectrum of 6a in dioxan was characterized by an absorption maximum at 280 nm (ϵ ,35,000).

B In Refluxing Benzene

In a repeat run, benzylideneacetone phenylhydrazone (1 g, 4.2 mmol) and nickel peroxide (3 g) were refluxed in benzene for 4 hr. Work-up of the mixture as in the previous case gave 0.45 g (45%) of 6a, mp 310° (mixture mp).

Oxidation of 2-Methylbenzylideneacetone Phenylhydrazone (1b)

Treatment of a mixture of 2-methylbenzylideneacetone phenylhydrazone (1.5 g, 6.0 mmol) and nickel peroxide (4.5 g)

in benzene (150 ml) for 3 hr at room temperature and work-up of the mixture in the usual manner gave a viscous liquid which was chromatographed over alumina. Elution with petroleum ether (bp 60-80°) gave 35 mg (4%) of biphenyl, mp 70° (mixture mp).

Further elution of the column with a mixture (1:2) of petroleum ether and benzene gave 0.55 g (36%) of meso-1,1'-diphenyl-3,3'-dimethyl-5,5'-di-(o-tolyl)-4,4'-bi-pyrazoline (7b), which melted at 257°, on recrystallization from a mixture (1:1) of benzene and alcohol.

Anal. Calcd for $C_{34}H_{34}N_4$: C, 81.93; H, 6.83; N, 11.24; Mol. wt.,498. Found: C, 81.79; H, 7.28; N, 11.04; Mol. wt.,498 (mass spectrometry).

The uv spectrum ($CHCl_3$) of 7b was characterized by an absorption maximum at 289 nm (ϵ ,39,500).

Oxidation of 3-Methylbenzylideneacetone Phenylhydrazone (1c)

A mixture of 3-methylbenzylideneacetone phenylhydrazone (1 g, 4.0 mmol) and nickel peroxide (3.5 g) was stirred in benzene (125 ml) for 3 hr at room temperature. Work-up of the mixture as in the earlier cases gave a red viscous liquid which was chromatographed over alumina. Elution of the column with petroleum ether gave 35 mg (6%) of biphenyl, mp and mmp 70°. Further elution of the column with a mixture (1:1) of petroleum ether and benzene gave a product, which on recrystallization from a mixture of benzene and alcohol gave 0.2 g (20%) of meso-1,1'-diphenyl-3,3'-dimethyl-5,5'-di-(m-tolyl)-4,4'-bipyrazoline (7c), mp 189-90°.

Anal. Calcd for $C_{34}H_{34}N_4$: C, 81.93; H, 6.83; N, 11.24; Mol. wt., 498. Found: C, 81.60; H, 6.70; N, 11.50; Mol. wt. 498 (mass spectrometry).

The uv spectrum (cyclohexane) of 7c was characterized by the following absorption maxima 220 nm (ϵ, 34,900) and 282 (43,100).

Further elution of the column with a mixture of benzene and petroleum ether gave a product which was recrystallized from benzene-alcohol mixture (2:1) to give 75 mg (8%) of dl-1,1'-diphenyl-3,3'-dimethyl-5,5'-di-(m-tolyl)-4,4'-bipyrazoline (6c), mp 285-86°.

Anal. Calcd for $C_{34}H_{34}N_4$: C, 81.93; H, 6.83; N, 11.24; Mol. wt., 498. Found: C, 81.69; H, 6.82; N, 11.21; Mol. wt., 498 (mass spectrometry).

The uv spectrum of 6c in chloroform showed an absorption maximum at 294 nm (ϵ, 18,400).

Oxidation of 4-Methylbenzylideneacetone Phenylhydrazone (1d)

A mixture of 4-methylbenzylideneacetone phenylhydrazone (1.5 g, 6.0 mmol) and nickel peroxide (3.5 g) was stirred in benzene (150 ml) for 4 hr at room temperature. Removal of the inorganic material and of the solvent gave a product which on recrystallization from benzene-ethanol mixture (1:1) gave 0.55 g (40%) of meso-1,1'-diphenyl-3,3'-dimethyl-5,5'-di-(p-tolyl)-4,4'-bipyrazoline (7d), mp 249°.

Anal. Calcd for $C_{34}H_{34}N_4$: C, 81.93; H, 5.83; N, 11.24; Mol. wt., 498. Found: C, 82.19; H, 5.95; H, 11.23; Mol. wt., 498 (mass spectrometry).

The uv spectrum (dioxan) of 7d showed an absorption maximum at 284 nm (ε ,39,700).

Oxidation of 2-Chlorobenzylideneacetone Phenylhydrazone (1e)

2-Chlorobenzylideneacetone phenylhydrazone (1 g, 3.7 mmol) and nickel peroxide (3 g) were stirred in benzene (125 ml) for 4 hr at room temperature. Work-up of the mixture in the usual manner gave a red viscous liquid which was chromatographed on alumina. Elution with petroleum ether gave 35 mg (6%) of biphenyl, mp 70° (mixture mp).

Further elution of the alumina column with a mixture (4:1) of petroleum ether and benzene gave a product which was recrystallized from a mixture (1:1) of benzene and alcohol to give 0.18 g (18%) of meso-1,1'-diphenyl-3,3'-dimethyl-5,5'-di-(o-chlorophenyl)-4,4'-bipyrazole (7e), mp 233-34°.

Anal. Calcd for $C_{32}H_{28}N_4Cl_2$: C, 71.24; H, 5.19; N, 10.39; Mol. wt.,539. Found: C, 70.85; H, 5.30; N, 10.16; Mol. wt.,539 (mass spectrometry).

The uv spectrum (cyclohexane) of 7e was characterized by the following absorption maximum at 279 nm(ε,31,400).

Oxidation of 3-Chlorobenzylideneacetone Phenylhydrazone (1f)

A mixture of 3-chlorobenzylideneacetone phenylhydrazone (1 g, 3.7 mmol) and nickel peroxide (3 g) was stirred in dry benzene (125 ml) for 4 hr at room temperature. Work-up of the mixture gave a viscous liquid which on treatment with ethanol yielded a solid material. The ethanolic

filtrate was worked up separately. Recrystallization of the solid product from a mixture (1:1) of benzene and ethanol gave 75 mg (8%) of dl-1,1'-diphenyl-3,3'-dimethyl-5,5'-di(m-chlorophenyl)-4,4'-bipyrazoline (6f), mp 246-47°.

Anal. Calcd for $C_{32}H_{28}N_4Cl_2$: C, 71.24; H, 5.19; N, 10.39; Mol. wt.,539. Found: C, 71.11; H, 4.91; N, 10.19; Mol. wt.,539 (mass spectrometry).

The uv spectrum (chloroform) of 6 showed an absorption maximum at 292 nm (ϵ ,36,000).

The ethanolic filtrate after removal of the crude 6f, was chromatographed on alumina. Elution with petroleum ether gave 30 mg (5%) of biphenyl, mp 70° (mixture mp). Further elution of the column employing a mixture (4:1) of benzene and petroleum ether gave a product, which on recrystallization from alcohol containing traces of benzene gave 0.25 g (25%) of meso-1,1'-diphenyl-3,3'-dimethyl-5,5'-di-(m-chlorophenyl)-4,4'-bipyrazoline (7f), mp 235-36°.

Anal. Calcd for $C_{32}H_{28}N_4Cl_2$: C, 71.24; H, 5.19; N, 10.39; Mol. wt.,539. Found: C, 71.32; H, 5.47; N, 10.47; Mol. wt.,539 (mass spectrometry).

The uv spectrum (cyclohexane) of 7f showed an absorption maximum at 280 nm (ϵ ,33,300).

Oxidation of 4-Chlorobenzylideneacetone Phenylhydrazone (1g)

Stirring a mixture of 4-chlorobenzylideneacetone phenylhydrazone (1.5 g, 5.5 mmol) and nickel peroxide (4.5 g) in benzene (150 ml) for 4 hr at room temperature and work-up of the mixture as in the earlier cases gave a viscous liquid.

Treatment of this liquid with ethanol gave a solid product and some ethanol-soluble material. The solid product on recrystallization from benzene gave 0.13 g (9%) of dl-1,1'-diphenyl-3,3'-dimethyl-5,5'-di-(p-chlorophenyl)-4,4'-bipyrazoline (6g), mp 174-75°.

Anal. Calcd for $C_{32}H_{28}N_4Cl_2$: C, 71.24; H, 5.19; N, 10.39; Mol. wt.,539. Found: C, 71.08; H, 5.50; N, 10.07; Mol. wt.,539 (mass spectrometry).

The uv spectrum (methylene chloride) of 6g showed an absorption maximum at 290 nm (ϵ ,19,400).

The ethanol-soluble portion was chromatographed over alumina. Elution with petroleum ether gave 30 mg (3%) of biphenyl, mp 70° (mixture mp). Further elution of the column with a mixture (4:1) of benzene and petroleum ether gave a product which on recrystallization from benzene-alcohol mixture (1:1) gave meso-1,1'-diphenyl-3,3'-dimethyl-5,5'-di-(p-chlorophenyl)-4,4'-bipyrazoline (7g), mp 248-29°.

Anal. Calcd for $C_{32}H_{28}N_4Cl_2$: C, 71.24; H, 5.19; N, 10.39; Mol. wt.,539. Found: C, 70.98; H, 5.30; N, 10.22; Mol. wt.,539 (mass spectrometry).

Oxidation of Furfurylideneacetone Phenylhydrazone (1h)

Furfurylideneacetone phenylhydrazone (1.5 g, 6.6 mmol) and nickel peroxide (4 g) were stirred in benzene (150 ml) at room temperature for 45 minutes. Work-up of the mixture in the usual manner gave a viscous material which was chromatographed on alumina. Elution with petroleum ether gave 40 mg (4%) of biphenyl, mp 70° (mixture mp). Further

elution of the column with a mixture (1:2) of petroleum ether and benzene gave a product which was recrystallized from alcohol to give 90 mg (6%) of meso-1,1'-diphenyl-3,3'-dimethyl-5,5'-di-(2-furyl)-4,4'-bipyrazoline (7h), mp 207-208°.

Anal. Calcd for $C_{28}H_{26}N_4O_2$: C, 74.66; H, 5.88; N, 12.44; Mol. wt.,450. Found: C, 74.49; H, 5.90; N, 12.45; Mol. wt.,450 (mass spectrometry).

Oxidation of Piperonylideneacetone Phenylhydrazone (1i)

Piperonylideneacetone phenylhydrazone (1.5 g, 5.3 mmol) and nickel peroxide (4.5 g) were stirred in benzene (150 ml) at room temperature for 5 hr. Work-up of the mixture gave a viscous liquid which was chromatographed on alumina. Elution with petroleum ether gave 62 mg (7%) of biphenyl, mp 70° (mixture mp). Further elution with a mixture (1:1) of benzene and petroleum gave a product which on recrystallization from benzene-alcohol mixture gave 0.45 g (30%) of meso-1,1'-diphenyl-3,3'-dimethyl-5,5'-di-piperonyl-4,4'-bipyrazoline (7i), mp 280-81°.

Anal. Calcd for $C_{34}H_{30}N_4O_4$: C, 73.12; H, 5.37; N, 10.03; Mol. wt.,558. Found: C, 73.43; H, 5.61; N, 10.00; Mol. wt.,558 (mass spectrometry).

The uv spectrum (chloroform) of 7i showed a characteristic absorption maximum at 288 nm (ϵ ,40,400).

Further elution of the column employing benzene as the eluent gave a product which on recrystallization afforded 0.2 g (14%) of dl-1,1'-diphenyl-3,3'-dimethyl-5,5'-dipiperonyl-

4,4'-bipyrazoline (6i), mp 270-71°.

Anal. Calcd for $C_{34}H_{30}N_4O_4$: C, 73.12; H, 5.37; N, 10.03; Mol. wt.,558. Found: C, 73.43; H, 5.10; N, 9.93; Mol. wt.,558 (mass spectrometry).

The uv spectrum (chloroform) showed an absorption maximum at 294 nm (ϵ,28,100).

Attempted Oxidation of dl-1,1',5,5'-Tetraphenyl-3,3'-dimethyl-4,4'-bipyrazoline (6a)

A With Nickel Peroxide

A mixture of 94 mg (0.2 mmol) of 6a and 0.3 g of nickel peroxide was refluxed in benzene for 3 hr. Work-up of the mixture gave 85 mg (90%) of the unchanged starting material 6a, mp 310° (mixture mp).

B With Sulfur

A mixture of 94 mg (0.2 mmol) of 6a and 0.15 g of sulfur was heated gradually in a test-tube to 200°, in an oil bath. After 2 hr, the reaction mixture was extracted with hot benzene. Removal of the solvent and recrystallization gave 70 mg (75%) of unchanged 6a, mp 310° (mixture mp).

C With Chloranil

A mixture of 94 mg (0.2 mmol) of 6a with 100 mg of chloranil was refluxed in dry xylene (50 ml) for 10 hr. After removal of the insoluble material, the xylene-soluble portion was washed with a 4% solution of potassium hydroxide and dried over anhydrous sodium sulfate. Removal of the solvent under vacuum gave 80 mg (85%) of unchanged starting material 6a, mp 310° (mixture mp) after recrystallization.

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CHAPTER III

OXIDATION OF BISPHENYL-HYDRAZONES OF 1,2-DIKETONES WITH NICKEL PEROXIDE

III.1 ABSTRACT

The oxidation of glyoxal bisphenylhydrazone, in benzene with nickel peroxide at room temperature, gives bisphenylazoethylene. Similarly, the oxidation of benzil bisphenylhydrazone, anisyl bisphenylhydrazone, 4,4'-dichlorobenzil bisphenylhydrazone and acenaphthenequinone bisphenylhydrazone, gives the corresponding bisphenylazoolefins. In addition, triazoles are also obtained in the oxidation of benzil bisphenylhydrazone and anisyl bisphenylhydrazone. The oxidation of methylglyoxal bisphenylhydrazone, gives a mixture of bisphenylazoolefin and phenylazopyrazole. Similarly, product mixtures consisting of bisphenylazoolefin and phenylazopyrazoles are obtained in the oxidation of both biacetyl bisphenylhydrazone and phenylmethylglyoxal bisphenylhydrazone. The oxidation of phenylglyoxal bisphenylhydrazone, on the other hand, gives a mixture of

2,5-diphenyl-1,2,3-triazole and 2,3,5,6-tetraphenyl-1,2,4,5-tetraazapentalene.

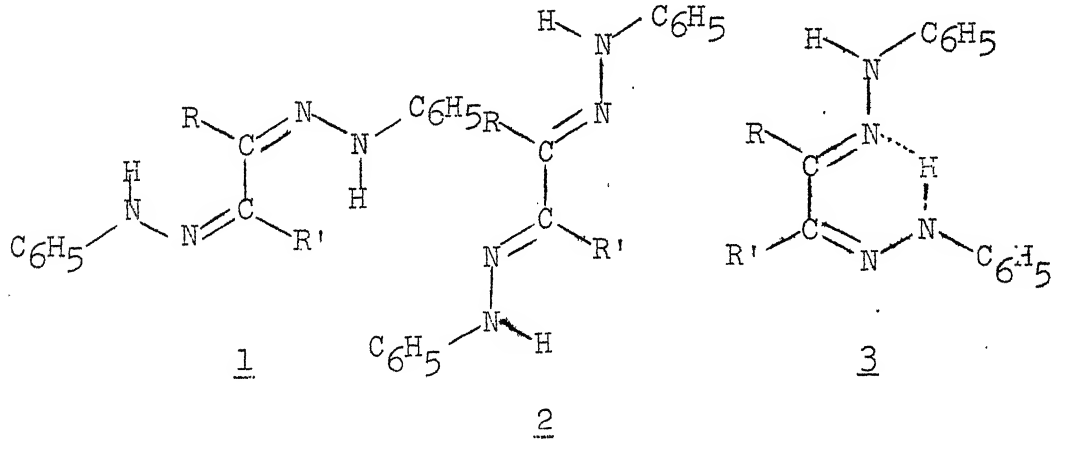
III.2 RESULTS AND DISCUSSION

In continuation of our studies concerning the oxidation of benzylideneacetone phenylhydrazones employing nickel peroxide, we have examined the oxidation of bisphenylhydrazones of 1,2-diketones using this reagent.

Bisphenylhydrazones of 1,2-diketones have been oxidized by a variety of reagents to give different products depending on the reaction conditions and also on the nature of the oxidizing agents. As for example, glyoxal bisphenylhydrazone has been reported to give bisphenylazoethylene, on oxidation with copper sulfate at room temperature.[1] Under refluxing conditions, however, 2-phenyl-1,2,3-triazole is formed in this reaction. When the oxidation is carried out using manganese dioxide, bisphenylazoethylene is the only product isolated both at room temperature and under refluxing conditions.[2] Similarly, biacetyl bisphenylhydrazone on oxidation with potassium dichromate and acetic acid gives 2,3-bisphenylazobut-2-ene.[3] The same product is obtained on oxidation with manganese dioxide at room temperature. Under refluxing conditions, however, the product formed is 1-phenyl-3-methyl-4-phenylazopyrazole.[2] Other oxidizing agents that have been successfully employed in the oxidation of bisphenylhydrazones of 1,2-diketones include alkaline potassium ferricyanide[4] and a mixture of iodine and sodium ethoxide.[5] Osotriazoles have been

reported to be formed in the oxidation of sugar osazones with reagents like copper sulfate,[6] nitrosodisulfonate,[6] and the halogens, chlorine, bromine and iodine.[6]

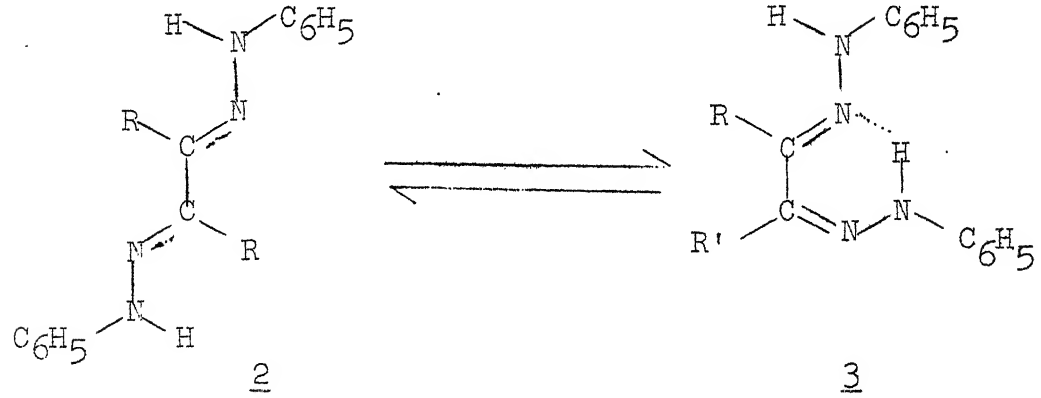
Considerable controversy exists in the literature concerning the structure of bisphenylhydrazones of 1,2-diketones and sugar osazones.[6,7] The three possible geometrical isomers of bisphenylhydrazones of 1,2-diketones are the syn-syn form (1), the anti-anti form (2), and the syn-anti form (3). In a detailed investigation employing nmr, Chapman and coworkers[8] have examined the structures of several bisphenylhydrazones of 1,2-diketones and sugar osazones and have shown that these compounds exist



1 2 3

either in the open chain anti-anti form (2) or in the cyclic, chelated form (3), depending upon the nature of the substituents R and R' and also of the polarity of the solvent medium. Thus, it has been observed that in the case of glyoxal bisphenylhydrazone, for example, the N-H protons appear as a sharp singlet at 10.35 δ in dimethyl sulfoxide medium, indicating thereby that the open chain

form 2 is favoured for this compound. Similarly, biacetyl bisphenylhydrazone also shows a single N-H proton signal at 9.25 δ indicating that its structure is analogous to that of glyoxal bisphenylhydrazone. In the case of cyclohexane-1, 2-dione bisphenylhydrazones, however, the nmr spectrum showed two N-H signals at 9.47 δ and 13.07 δ, in dimethyl sulfoxide, suggesting thereby that it exists in the chelated form 3. In general, it has been observed that under appropriate conditions, simple bisphenylhydrazones exist as equilibrium mixtures consisting of both the open-chain and chelated forms. The ratio of this equilibrium depends in part on the steric sizes of the substituents R and R' and also on the polarity of the solvent medium. Thus, when R and R' are relatively small, the open-chain form (2) is favoured, whereas the equilibrium shifts to the chelated form 3, as the sizes of R and R' increase. It has been



2 3

observed that sugar osazones, benzil bisphenylhydrazone[9] and other bisphenylhydrazones which contain bulky substituent groups exist chiefly in the chelated form, whereas glyoxal bisphenylhydrazone and biacetyl bisphenylhydrazone which

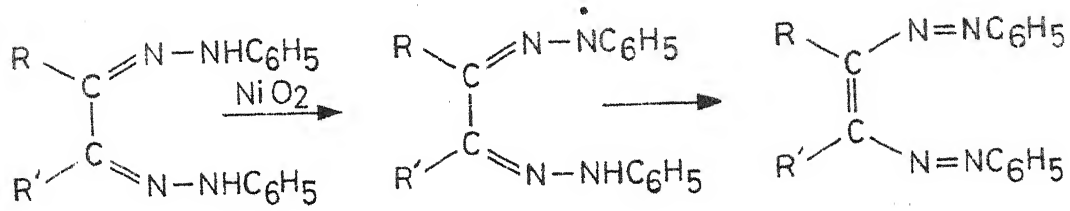
contain small substituent groups exist predominantly in the non-chelated form.

During the course of the present investigation, we have studied the oxidation of several bisphenylhydrazones of 1,2-diketones with a view to finding out whether the products formed in these oxidations bear any relation to the structure of the starting bisphenylhydrazones. Treatment of glyoxal bisphenylhydrazone (4a) with nickel peroxide, at room temperature in benzene solution, gives a 93% yield of bisphenylazoethylene (6a). It might be mentioned in this connection that von Pechmann[3a] has assigned a dihydrotetrazine structure for the oxidation product of glyoxal bisphenylhydrazone. However, subsequent studies have shown that these compounds are in fact bisazoolefins.[3b] This view is further supported by spectroscopic evidences[10] and also by studies on liquid crystals.[11]

A probable route to the formation of 6a in the oxidation of 4a is shown in Scheme III.1. In this scheme, we assume that nickel peroxide abstracts a hydrogen atom from glyoxal bisphenylhydrazone giving rise to a radical intermediate 5. Further loss of a hydrogen atom from 5 leads to the bisazoolefin 6.

The oxidation of benzil bisphenylhydrazone (4b) with nickel peroxide at room temperature, on the other hand, gives a 71% yield of bisphenylazostilbene (6b) and a 13% yield of 2,4,5-triphenyl-1,2,3-triazole (8b). Under refluxing conditions, however, a 66% yield of 6b and a 13% yield

Scheme III·1

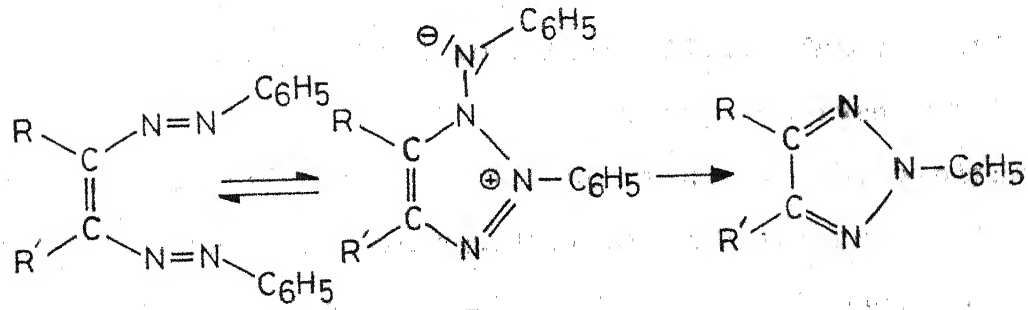


4 a, R=R′=H
b, R=R′=C6H5
c, R=R′=p-CH3OC6H4
d, R=R′=p-ClC6H4
e, R, R′= 

5

6 a, R=R′=H
b, R=R′=C6H5
c, R=R′=p-CH3OC6H4
d, R=R′=p-ClC6H4
e, R, R′= 

Scheme III·2



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6 b, R=R′=C6H5
c, R=R′=p-CH3OC6H4

8 b, R=R′=C6H5
c, R=R′=p-CH3OC6H4

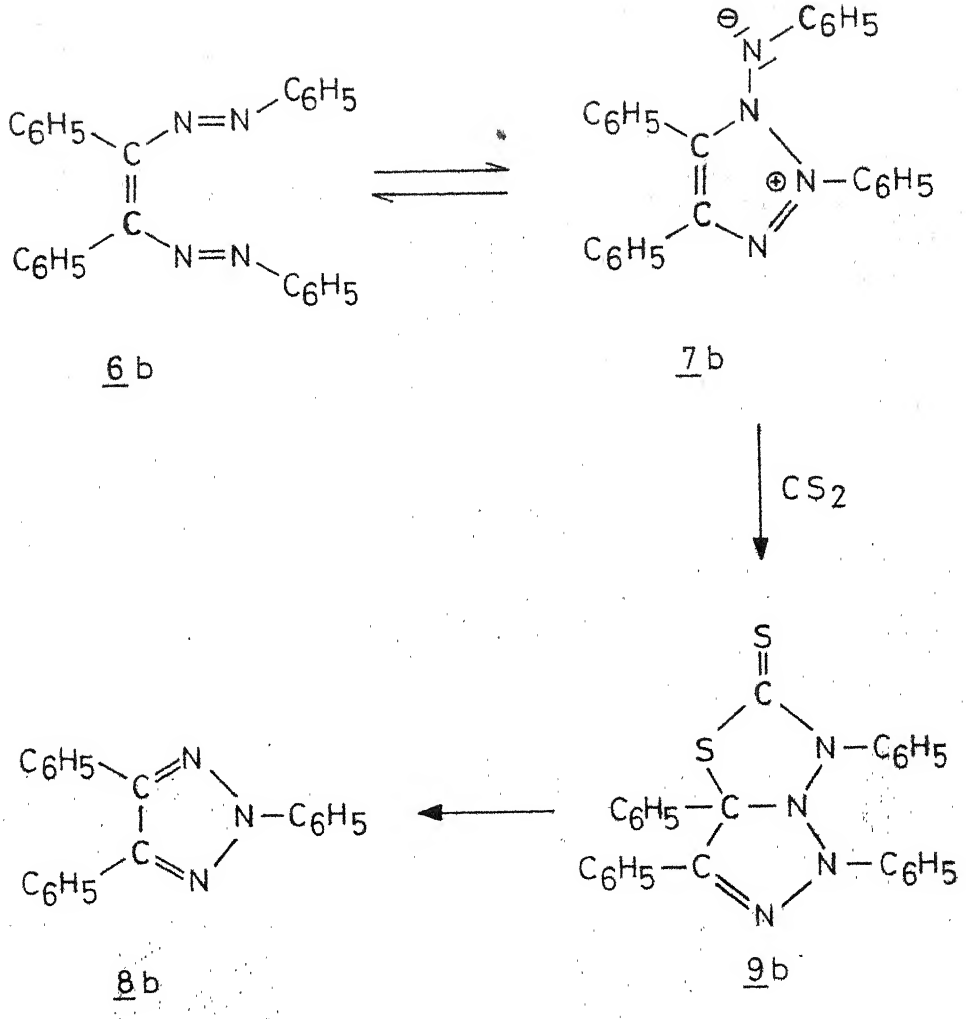
of 8b, together with traces of azobenzene are obtained. It might be mentioned in this connection that the oxidation of benzil bisphenylhydrazone with manganese dioxide[2] gives a mixture of biphenyl and the triazole 8b. No bisazoolefin could be isolated from this reaction. Similarly, the oxidation of anisyl bisphenylhydrazone (4c) at room temperature gives a 48% yield of bisphenylazostilbene (6c) and a 21% yield of 2-phenyl-4,5-dianisyl-1,2,3-triazole (8c). The room temperature oxidation of 4,4'-dichlorobenzil bisphenylhydrazone (4d) gives a 87% yield of the corresponding bisphenylazostilbene, as the only isolable product. The oxidation of acenaphthenequinone bisphenylhydrazone (4e), both at room temperature and under refluxing conditions gives, nearly quantitative yields of 1,2-bisphenylazoacenaphthalene (6e).

The formation of the bisphenylazostilbenes 6b-e in these oxidations can be rationalized in terms of a free radical process as shown in Scheme III.1. The formation of triazoles in these oxidations, however, deserves special mention. It has been recently pointed out that a bisazoolefin such as 6b can exist in equilibrium with the mesoionic form 7b (Scheme III.2) and that 7b undergoes cycloadditions with different dipolarophiles.[12a] The reaction of 6b with carbon disulfide resulted in the formation of a 83% yield of 2,4,5-triphenyl-1,2,3-triazole (8b), and a 51% yield of phenylisothiocyanate. In addition, a 83 % yield of elemental sulfur could also be isolated from this run. The formation

of these products can be explained through the intermediate 9, which undergoes further fragmentation as shown in Scheme III.3. It has also been shown that 7b can be transformed to the triazole 8b, through the loss of phenylnitrene, both under thermal and photochemical conditions.[12] It is therefore, assumed that the triazoles are formed in the oxidation of the bisphenylhydrazones of 1,2-diketones through the bis-azoolefins. The fact that triazoles are not formed in the cases of glyoxal bisphenylhydrazone and acenaphthenequinone bisphenylhydrazone would probably suggest that the bis-azoolefins formed in these cases do not exist in equilibrium with their corresponding mesoionic forms.

In continuation of our studies, we have examined the oxidation of the bisphenylhydrazones of few alkyl substituted glyoxal derivatives. Treatment of methylglyoxal bisphenylhydrazone (10a) with nickel peroxide, at room temperature, gives a 90% yield of 1,2-bisphenylazopropylene (12a), as the only isolable product. Under refluxing conditions, however, the products formed are a 3% yield of biphenyl, a 45% yield of 1,2-bisphenylazopropylene and a 15% yield of a product, identified as 1-phenyl-4-phenylazopyrazole (16a). A probable route to the formation of products such as 12a and 16a in the oxidation of 10a is shown in Scheme III.4. In this scheme, we assume that 10a undergoes initial oxidation to the radical intermediate 11, which on further oxidation gives rise to the bisphenylazoolefin 12a. Another possible mode for the oxidation of 11 is through the phenyl-

Scheme III·3

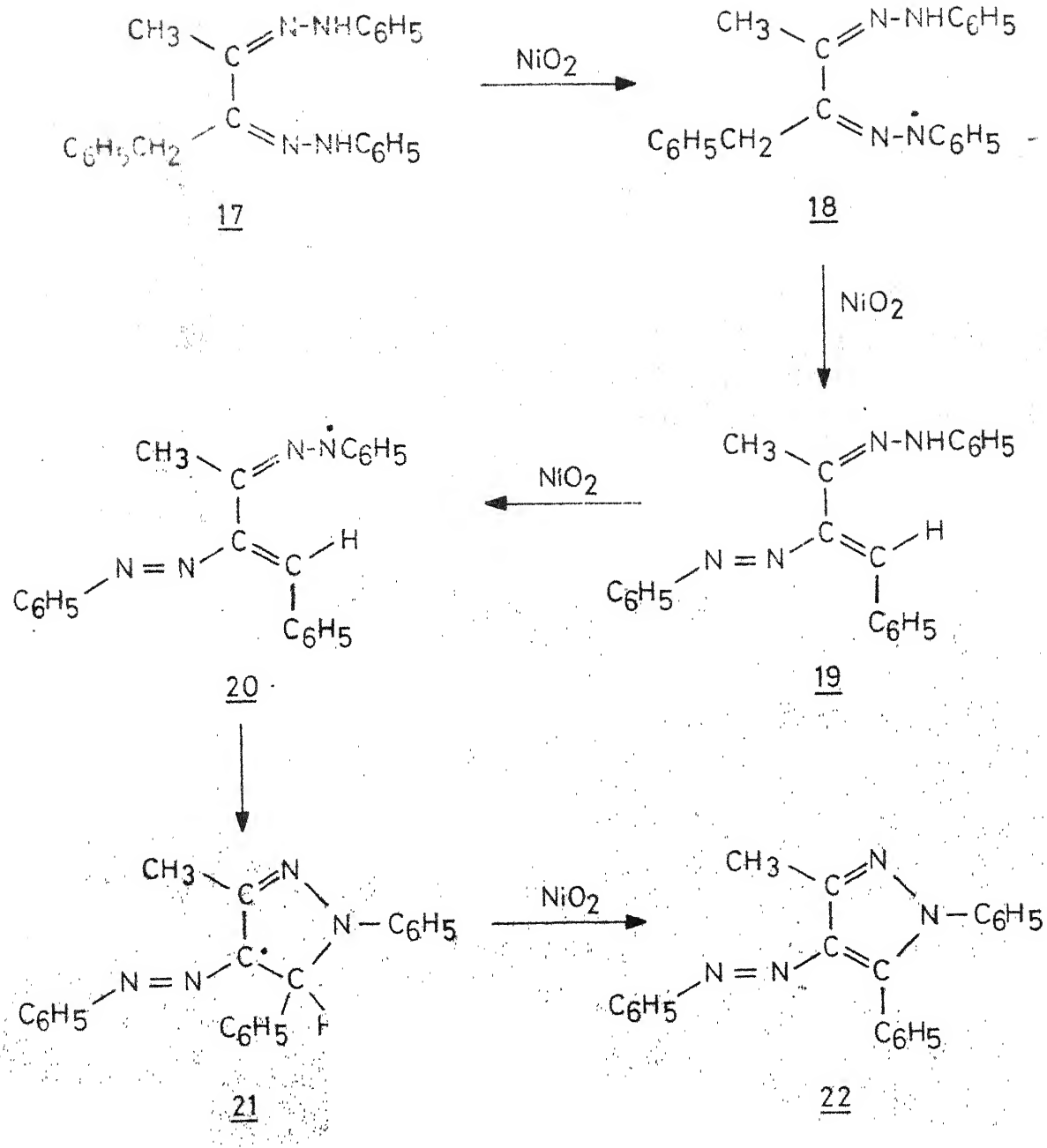


azoalkene intermediate 13, which can then undergo subsequent oxidative cyclization leading to the phenylazopyrazole 16a (Scheme III.4).

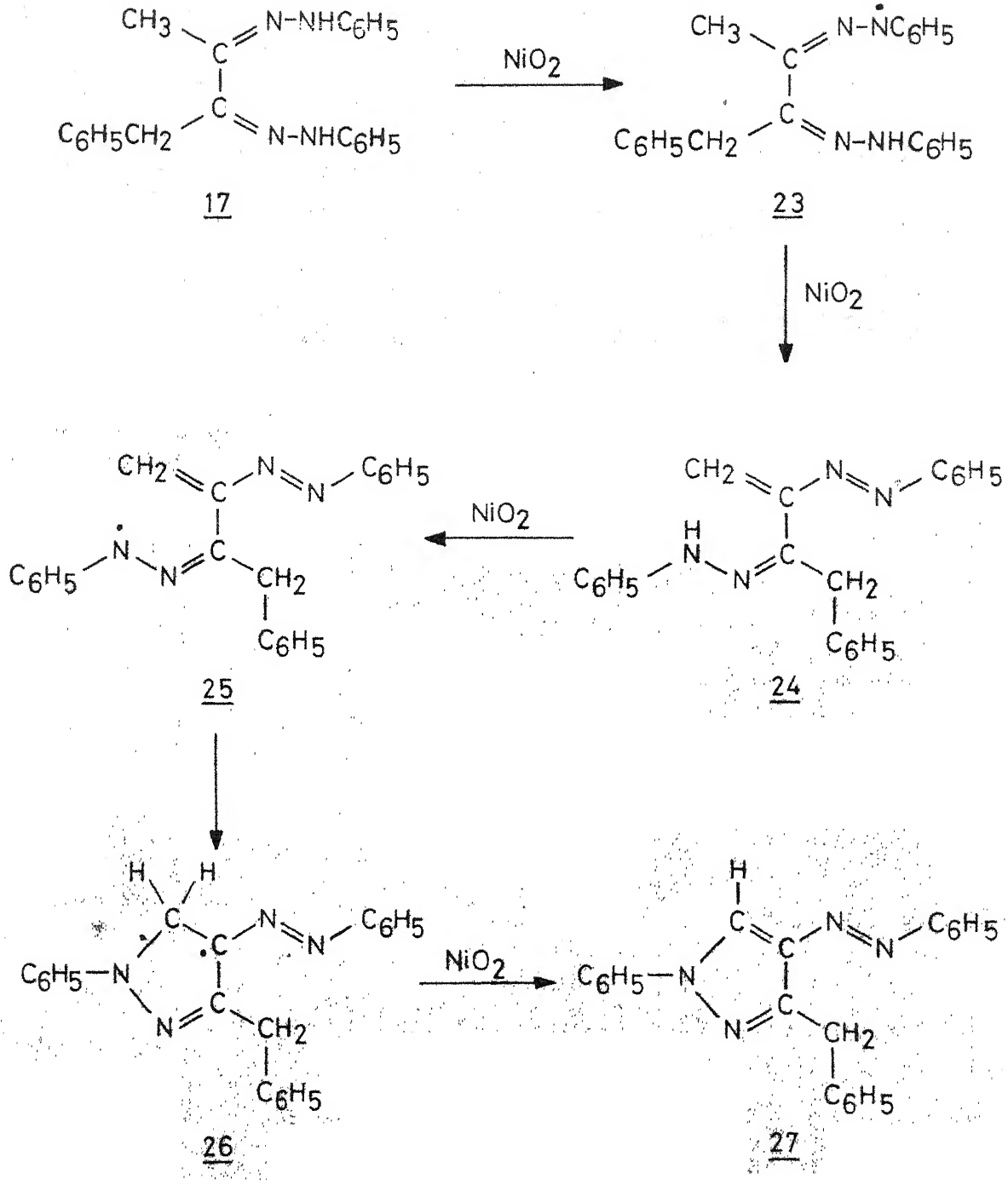
Similarly, the oxidation of biacetyl bisphenylhydrazone (10b) with nickel peroxide at room temperature gives a 85% yield of 2,3-bisphenylazobut-2-ene (12b). Under refluxing conditions, however, the products formed are biphenyl (6%) and 1-phenyl-3-methyl-4-phenylazopyrazole (16b) (52%). The oxidation of phenylmethylglyoxal bisphenylhydrazone (10c), on the other hand, gives the corresponding phenyl azopyrazole (16c) both at room temperature and under refluxing conditions. In addition to the azopyrazole, a small quantity of biphenyl is also isolated from the reaction, under refluxing conditions.

The room temperature-oxidation of benzylmethylglyoxal bisphenylhydrazone (17) with nickel peroxide gives a 50% yield of 1,5-diphenyl-3-methyl-4-phenylazopyrazole (20) and a 19% yield of a product identified as 3-phenylazo-3-buten-2-one phenylhydrazone 19 (Scheme III.5). The structure of 19 is established on the basis of elemental analysis, molecular weight and spectral evidences. The ir spectrum of 19 shows an absorption band at 1600 cm^{-1} due to a C=N group. The uv spectrum of 19 is characterized by the presence of strong absorption maxima at 240 nm (ϵ ,14,600), 280 (20,000), 348 (33,400) and a shoulder at 366 (23,900). The nmr spectrum of 19 (Figure III.1) in $CDCl_3$ shows signals at 2.17 δ(3H), 7.23 δ(17H) and 7.85 δ(1H) respectively. Of these, the sharp

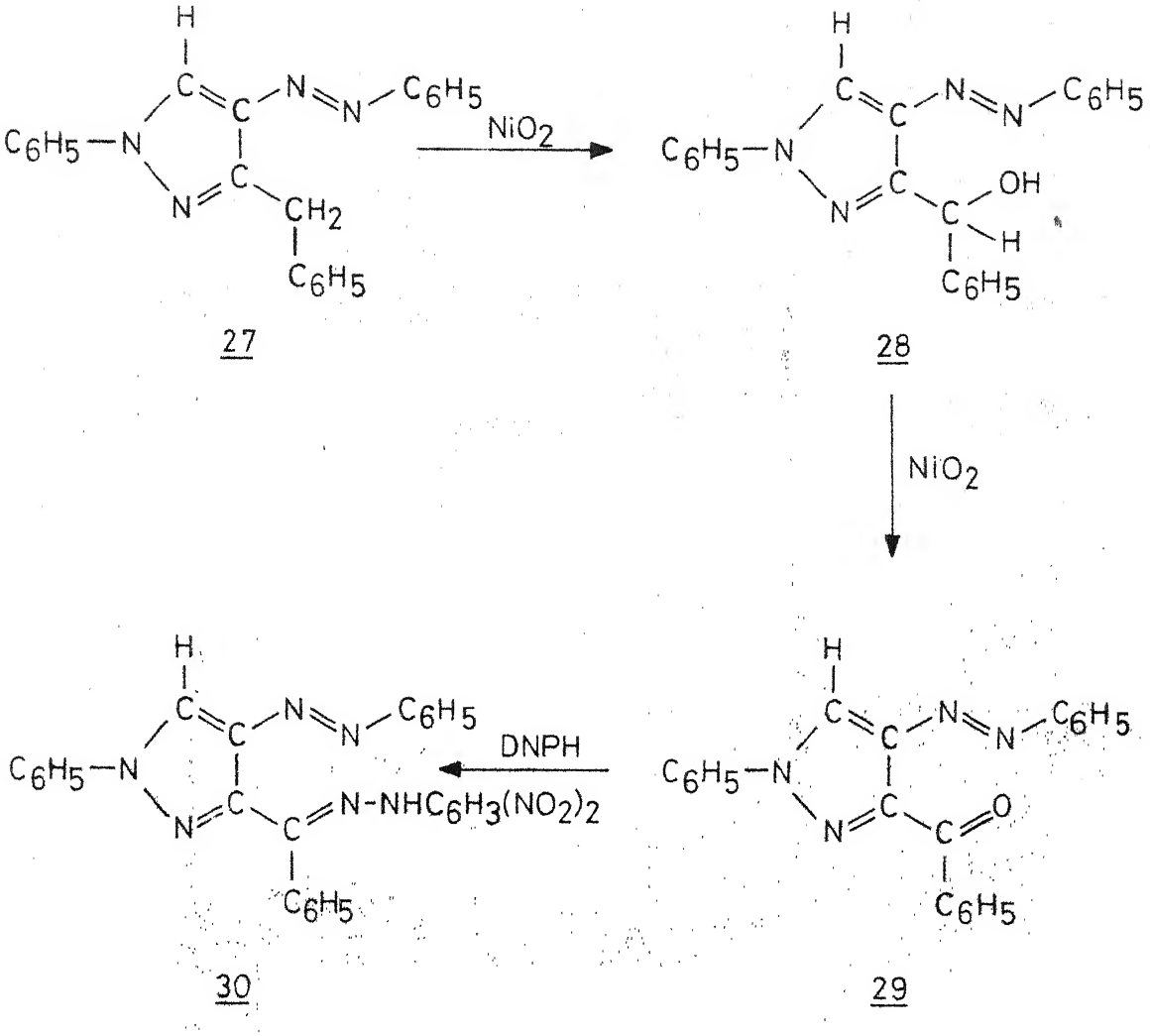
Scheme III·5


CH3
N-NHC6H5
C6H5CH2
N-NHC6H5
NiO2
17
18
19
20
21
22
N = N
C6H5
H
N-C6H5

Scheme III·5 (Contd.)



Scheme III·5 (Contd.)



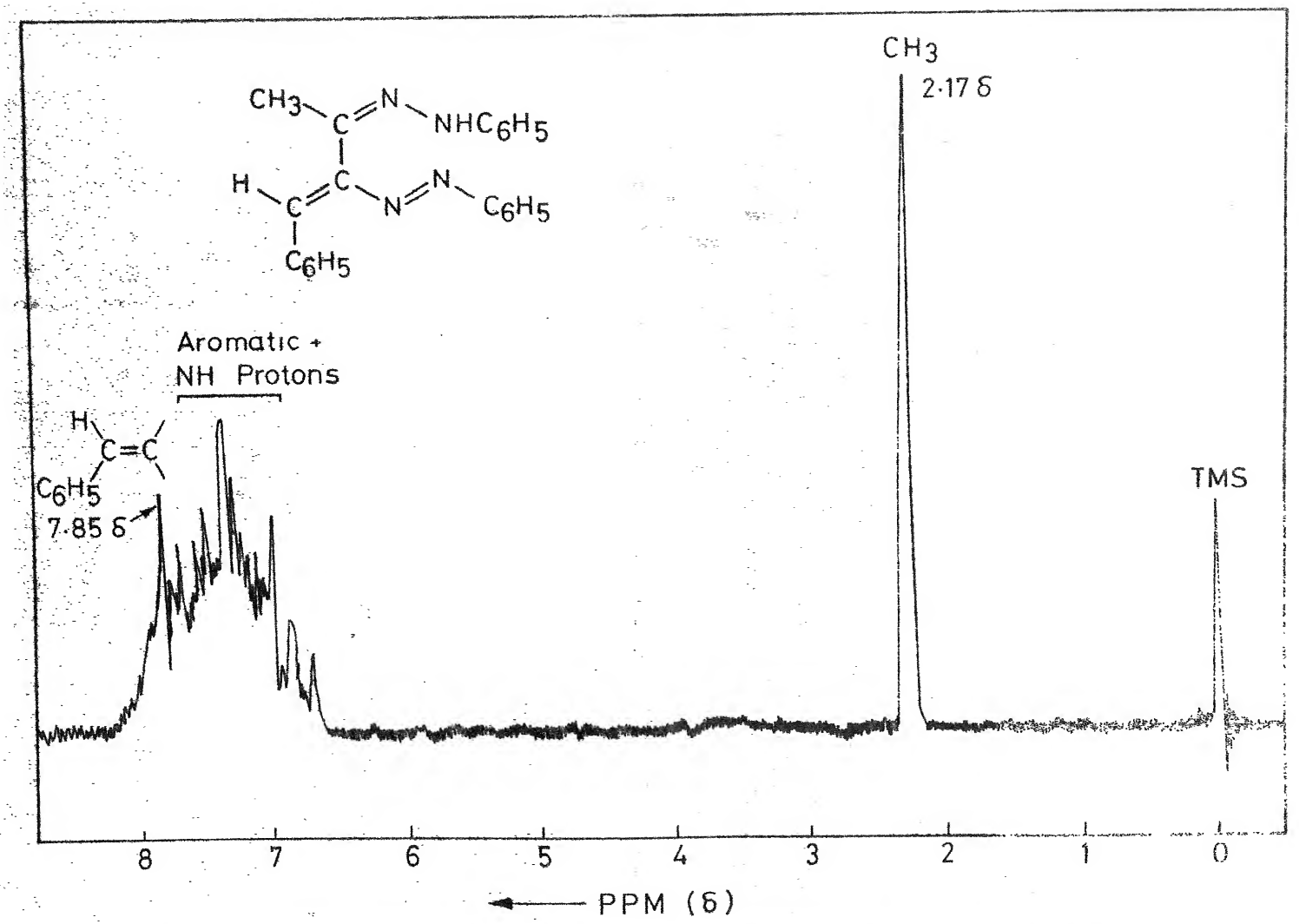


Fig.III.1 NMR spectrum (60MHz) of 3-phenylazo-3-buten-2-one phenylhydrazone (19)

singlet at 2.17 δ is assigned to the methyl proton, whereas, the multiplet centred around 7.23 δ is assigned to the aromatic protons. The N-H proton appears to be hidden underneath the aromatic protons. The vinylic proton appears as a singlet at 7.85 δ . Further confirmation of the structure of 19 is derived from the fact that it undergoes oxidative cyclization, on treatment with nickel peroxide to give 1,5-diphenyl-3-methyl-4-phenylazopyrazole (22).

Additional evidence concerning the structure of 19 is derived from electron impact studies. The mass spectrum of 19 (Figure III.2) shows the molecular ion peak at m/e 340. Other peaks are observed at m/e 338, 261, 248, 235, 233, 194, 180, 128, 116, 91 and 77 which may be due to some of the fragments shown in Scheme III.6. The species at m/e 338 is formulated as the ion corresponding to the phenylazo-pyrazole (19a). Loss of a phenyl group from 19a would result in the formation of the ion 19b, m/e 261, whereas, the loss of a nitrogen molecule from 19b leads to the pyrazole ion (19c), at m/e 233. Another mode of fragmentation of the molecular ion peak is through the loss of a phenylazo group resulting in the pyrazoline ion (19h) at m/e 235. The peak at m/e 248 can be ascribed to the triazolinium ion (19f) or the triazole ion (19g) formed through the loss of a C_6H_5NH group from the molecular ion. It might be pointed out that similar loss of C_6H_5-NH fragments leading to triazole formation has been observed in the mass spectra of bisazoalkanes.[13] The peak at m/e 128 is assigned to the fragment 19d. The peak at

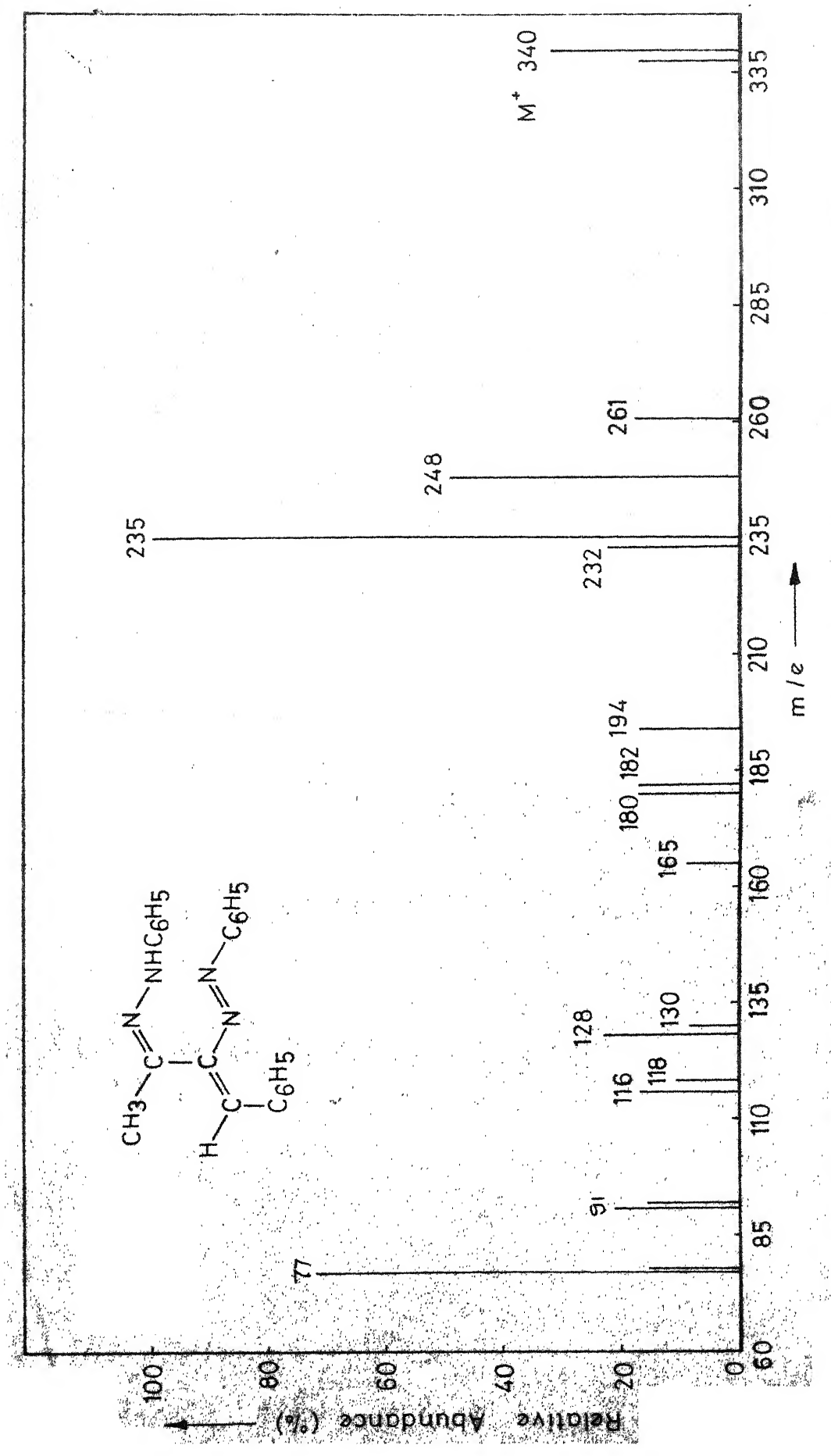
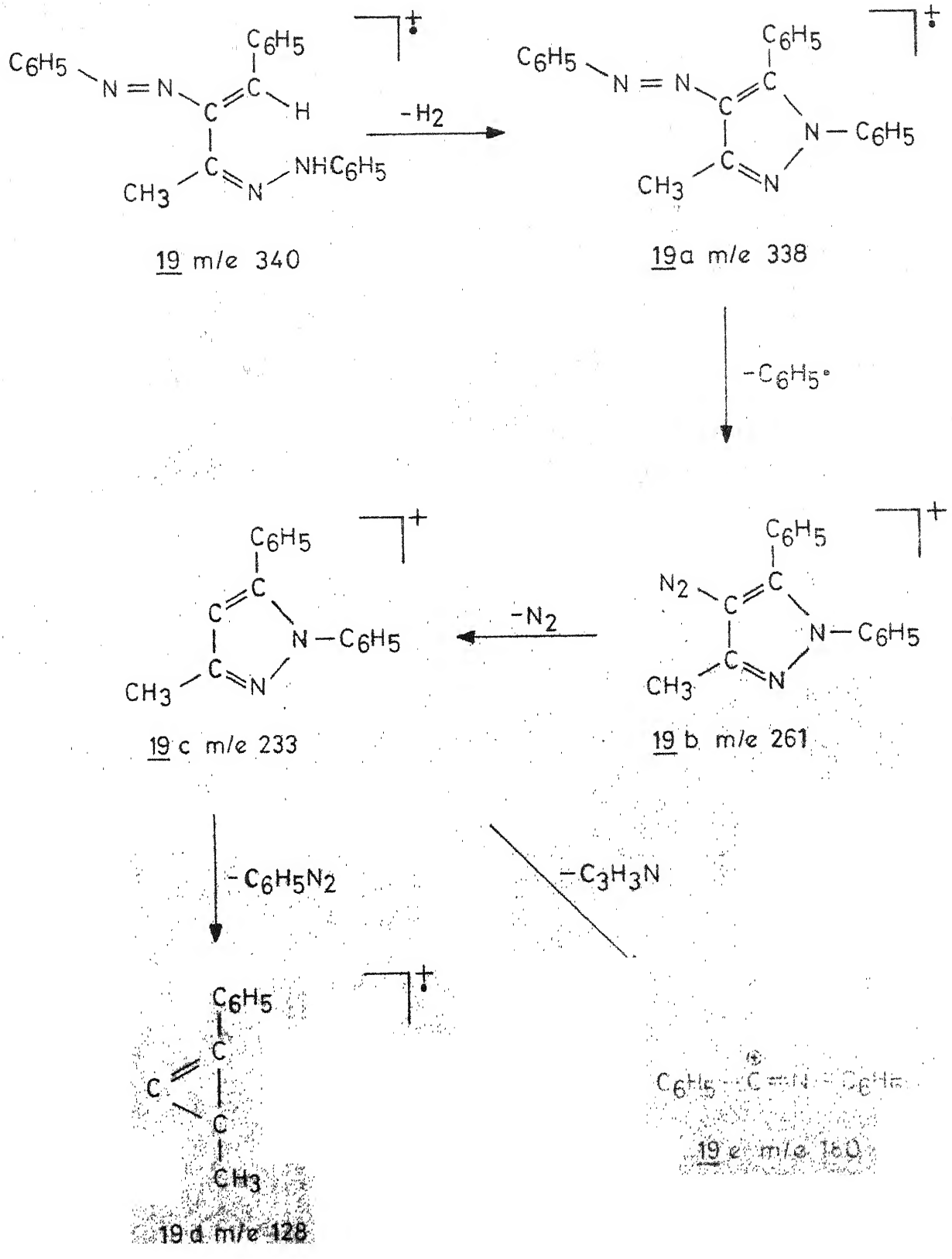


Fig.III.2 Mass spectrum of 3-phenylazo-3-buten-2-one phenylhydrazone (19)

Scheme III·6



19 m/e 340

19a m/e 338

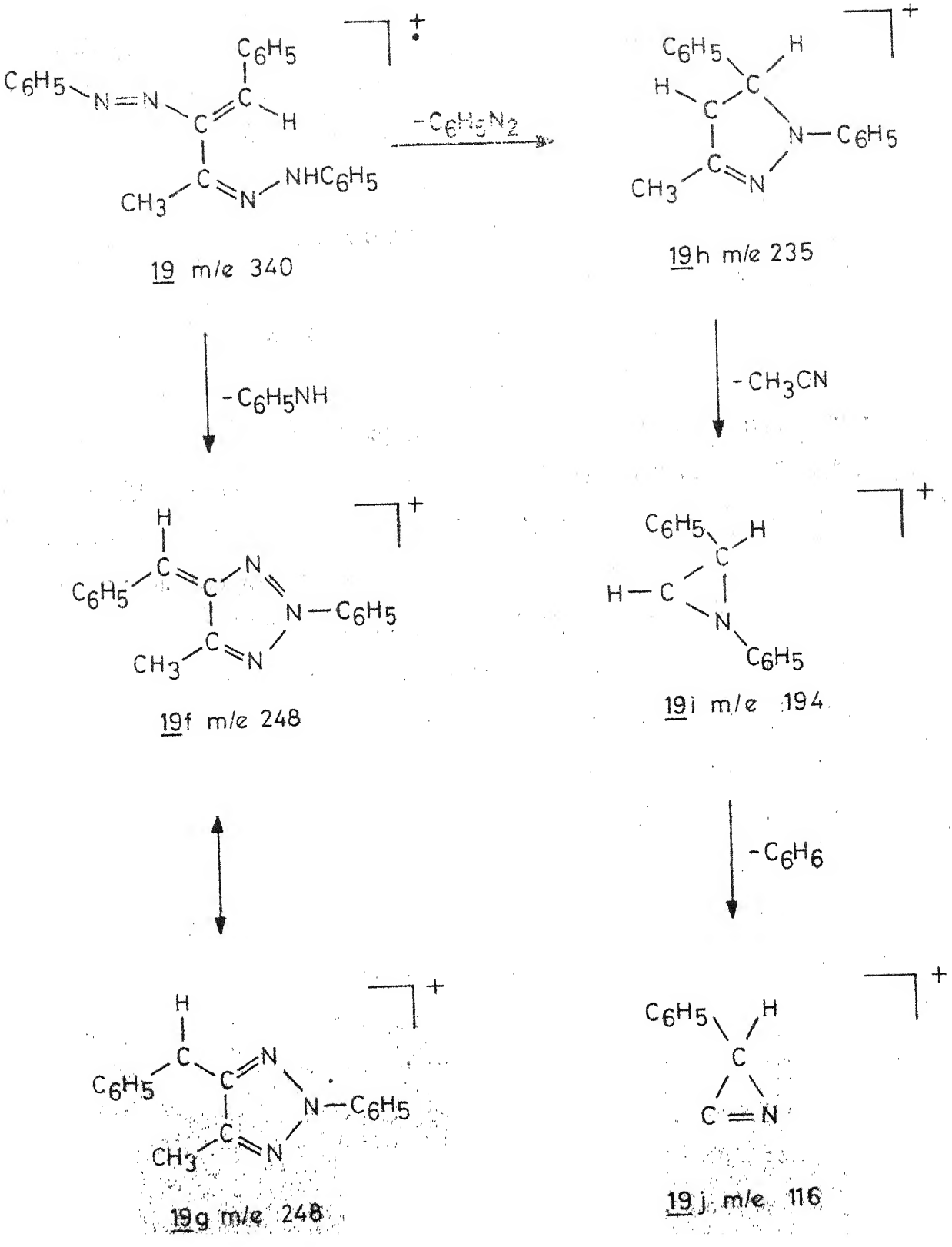
19 b m/e 261

19 c m/e 233

19 d m/e 128

19 e m/e 180

Scheme III·6 (Contd.)



m/e 180, on the other hand, could be due to the fragment 19e. The peaks at m/e 194 and m/e 116, could be assigned to 19i and 19j, arising through the successive loss of acetonitrile and benzene, respectively, from 19h.

The oxidation of benzylmethylglyoxal bisphenylhydrazone with nickel peroxide, under refluxing conditions, however, gives a 14% yield of 19, a 67% yield of the pyrazole derivative 22 and a 3% yield of a product melting at 153°, identified as 1-phenyl-3-benzoyl-4-phenylazopyrazole (29). The structure of (29) is arrived at on the basis of elemental analysis and spectral data. Elemental analysis has shown that 29 should have the molecular formula $C_{22}H_{16}N_4O$. The ir spectrum reveals the presence of a carbonyl group at 1665 cm^{-1}. The uv spectrum of 29 shows absorption maxima at 258 nm (ϵ ,21,700), 284 (17,200), 342 (13,400) and 424 (1,050), characteristic of 4-phenylazopyrazoles. Further confirmation of 29 has been derived from its conversion to a 2,4-dinitrophenylhydrazone derivative 30, melting at 242-243°.

Additional support regarding the structure of 29 is derived from electron impact studies. The mass spectrum of 29 (Figure III.3) shows the molecular ion peak at m/e 352. Othe peaks are observed at m/e 275, 247, 144, 116, 105 and 77, which could be assigned to some of the fragments shown in Scheme III.7. Loss of a phenyl group from the molecular ion would result in the formation of the ion 29a, which appears as the base peak at m/e 275. It might be mentioned in this connection that in the mass spectral fragmentation of 4-acetylpyrazole, the $[M-CH_3]^+$ ion is present as the base peak.[14]

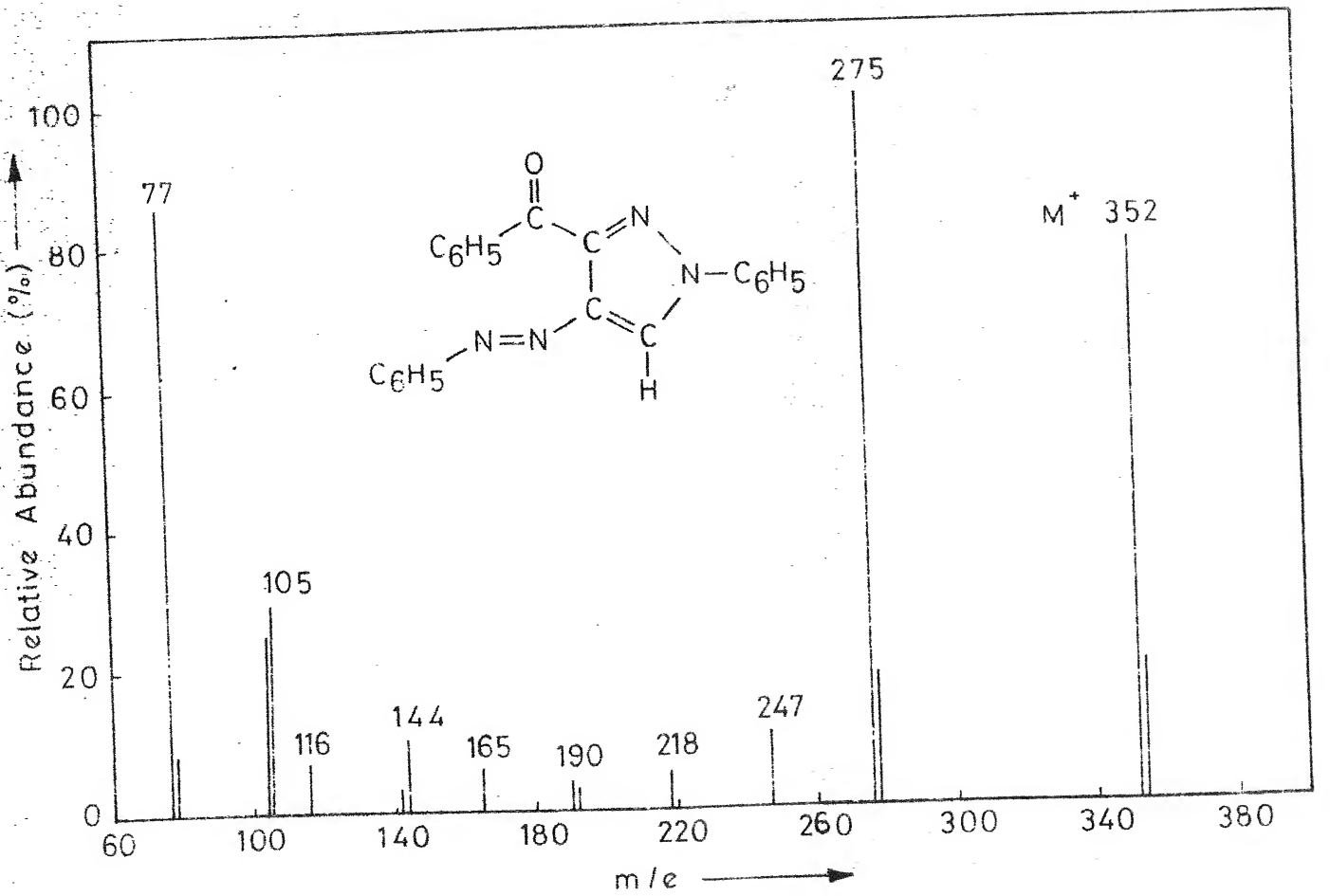
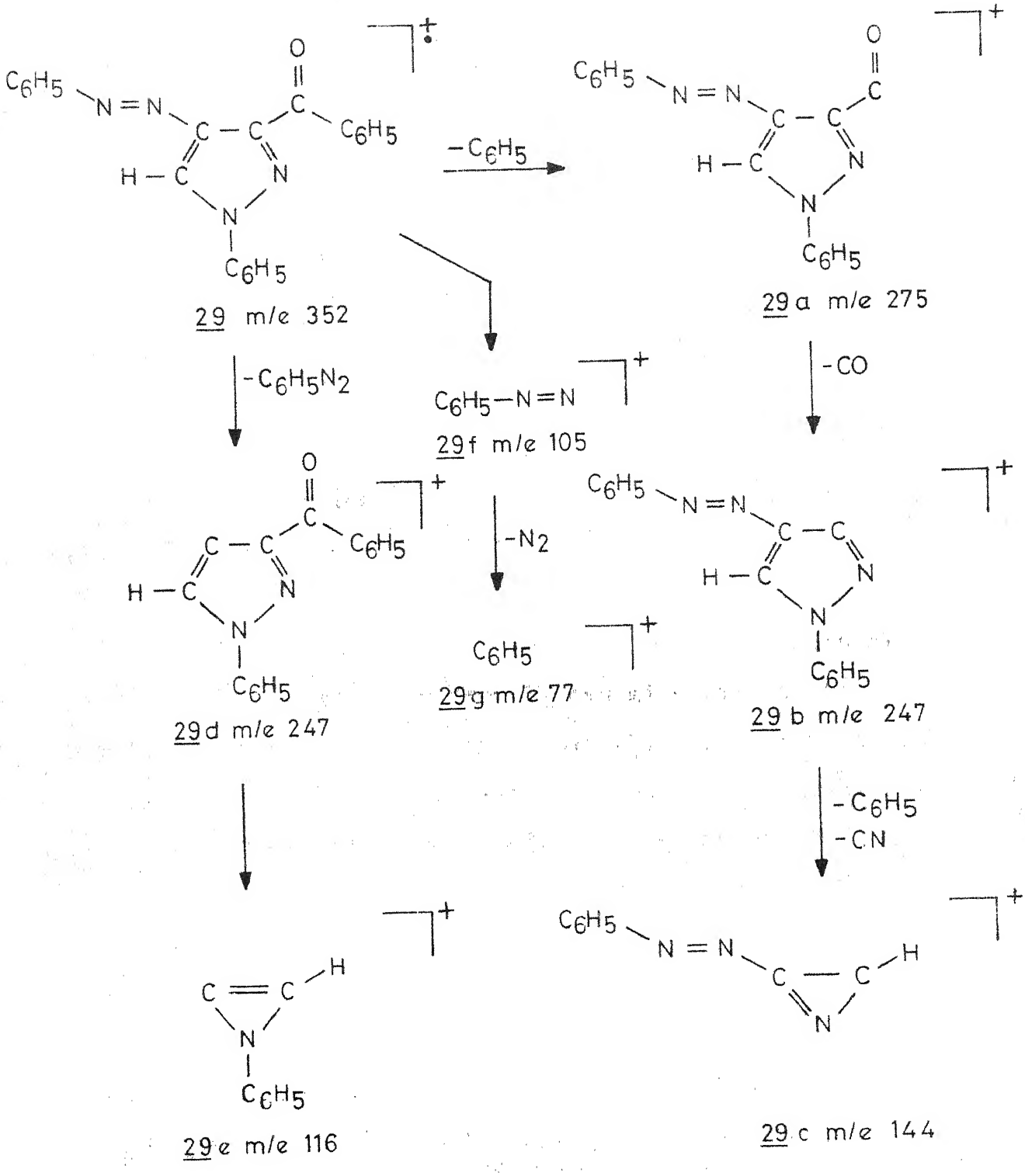


Fig.III.3 Mass spectrum of 1-phenyl-3-benzoyl-4-phenylazopyrazole (29)

Scheme III·7


29 m/e 352
-C6H5
29a m/e 275
-C6H5N2
C6H5-N=N
29f m/e 105
-CO
-N2
C6H5
29g m/e 77
29d m/e 247
29b m/e 247
-C6H5
-CN
29e m/e 116
29c m/e 144

Loss of carbon monoxide from 29a would result in the formation of the fragment 29b at m/e 247. The m/e 247 fragment could also be due to 29d, resulting from the loss of a phenylazo group from the molecular ion. The peak at m/e 144 could be assigned to 29c, derived through the loss of a C_6H_5CN fragment from 29b. Similarly, the loss of a C_6H_5COCN group from 29d would result in the fragment at m/e 116 (29e). The peak at m/e 105 could be due to the phenylazo group (29f) which can lose a molecule of nitrogen resulting in the formation of the fragment 29g, with m/e 77.

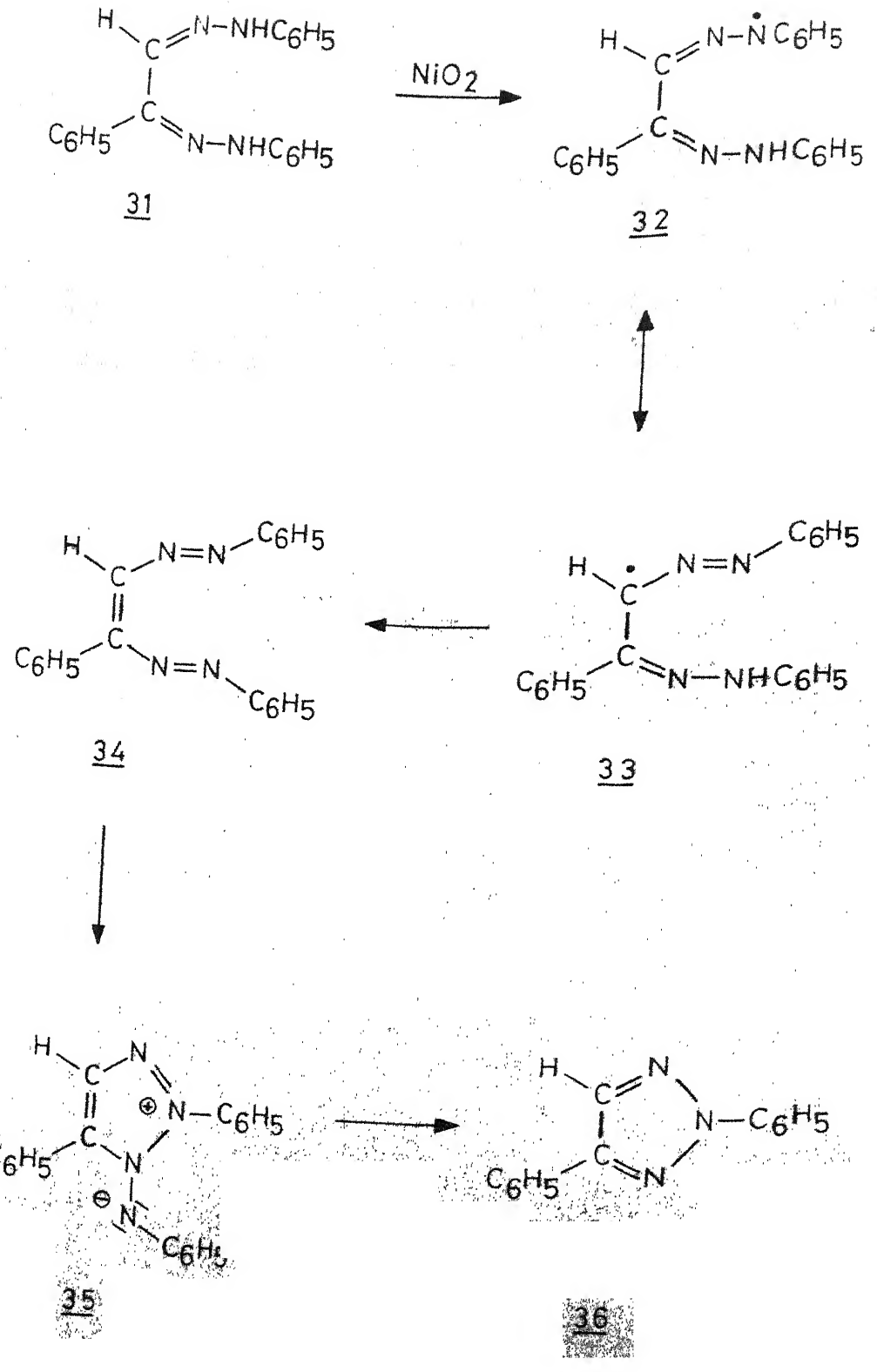
The formation of products such as 19, 22 and 29 in the oxidation of benzylmethylglyoxal bisphenylhydrazone may be rationalized in terms of the reaction sequences shown in Scheme III.5. In this scheme, we assume that the initial removal of a hydrogen atom from 17 can give rise to the radical intermediate 18 or its isomer 23. Further oxidation of 18 would result in the formation of the phenylazoalkene 19, which can undergo oxidative cyclization to the phenylazopyrazole 22, through the intermediates 20 and 21. Further oxidation of the radical intermediate 23, on the other hand, would lead to the phenylazoalkene 24, which can subsequently undergo oxidative cyclization to the phenylazopyrazole 27. It would be reasonable to assume that the methylene group in 27, will undergo further oxidation, in presence of nickel peroxide to the phenylazobenzoylpyrazole 29 through the carbinol 28 as shown in Scheme III.5. Such oxidations of methylene groups to the corresponding carbonyl derivatives

are commonly observed in the reactions with both manganese dioxide[15] and nickel peroxide.[16]

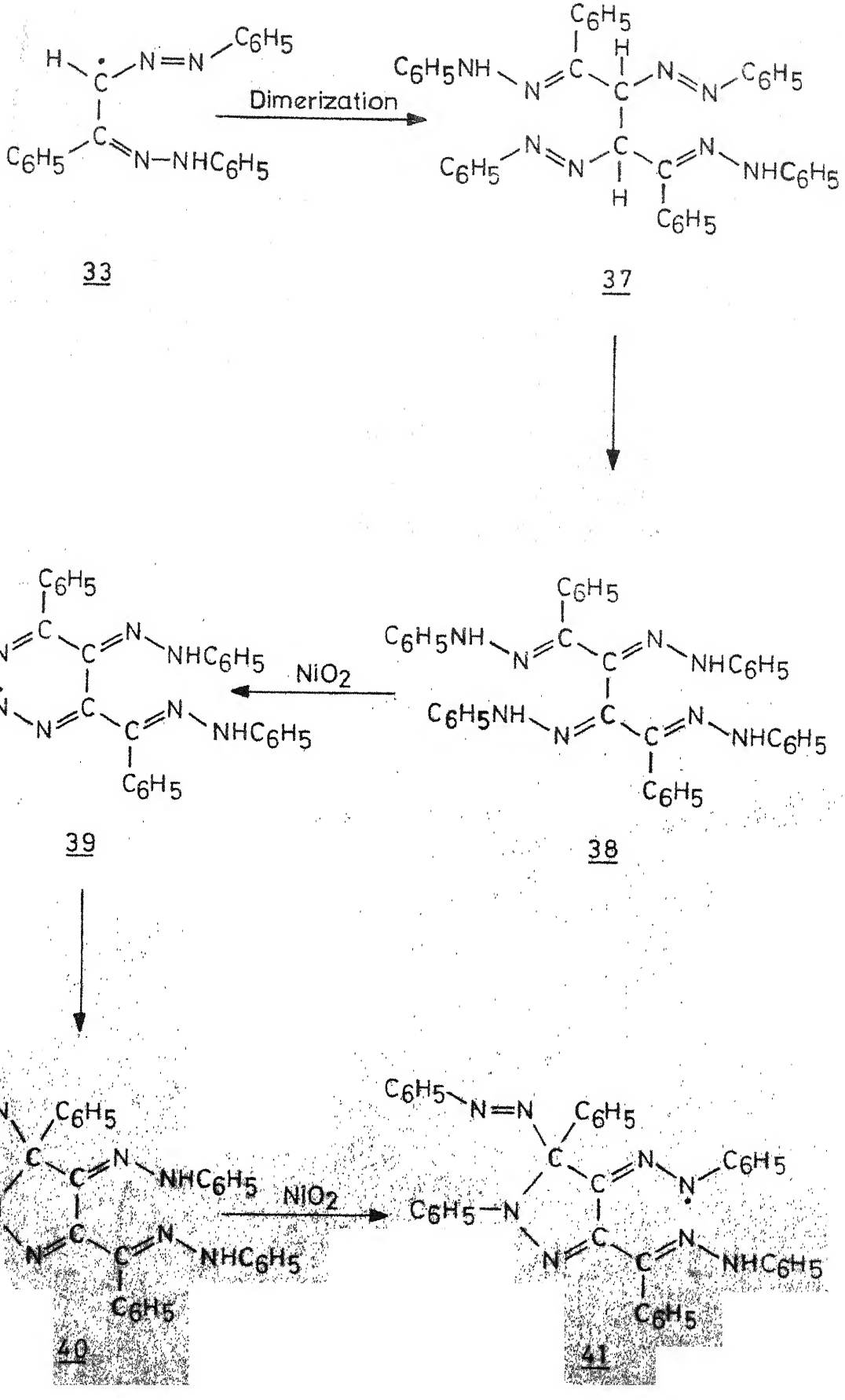
Oxidation of phenylglyoxal bisphenylhydrazone (31) with nickel peroxide in refluxing benzene gives a mixture of products consisting of biphenyl (20%) and 2,5-diphenyl-1,2,3-triazole (36) (19%). In addition, a 18% yield of a yellow compound melting at 315° and analysing for $C_{28}H_{20}N_4$ is also isolated from this reaction. The structure of this compound is established as 2,3,5,6-tetraphenyl-1,2,4,5-tetraazapentalene (43) on the basis of analytical data and spectral evidences. The mass spectrum of 43 shows a molecular ion peak at m/e 412. The ir spectrum of 43 does not show any free N-H group, whereas, the uv spectrum shows two intense absorption maxima at 278 nm and 386 nm, respectively. The analytical data and spectral characteristics of 43 correspond to an analogous compound, obtained from the reaction of silver phenylacetylide with p-chlorobenzenediazonium chloride.[17]

The formation of the triazole 36 and the tetraazapentalene derivative 43 in the oxidation of phenylglyoxal bisphenylhydrazone (31) may be rationalized in terms of the route shown in Scheme III.8. We assume that the initial oxidation product of 31 is the radical intermediate 32, which then is further oxidized to the bisphenylazoolefin 34. The bisphenylazoolefin 34 can then be converted to the triazole 36 through the loss of phenylnitrene from the mesoionic intermediate 35. The formation of the tetraaza-

Scheme III.8

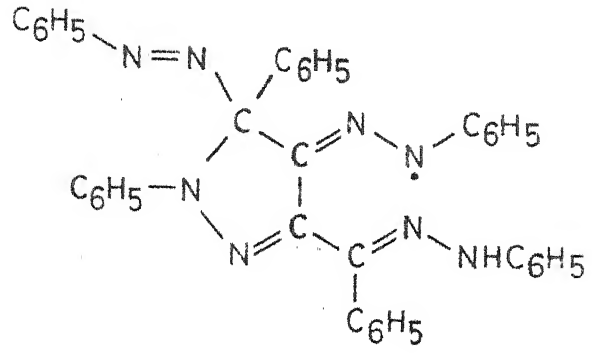


Scheme III·8 (Contd.)

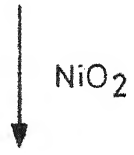


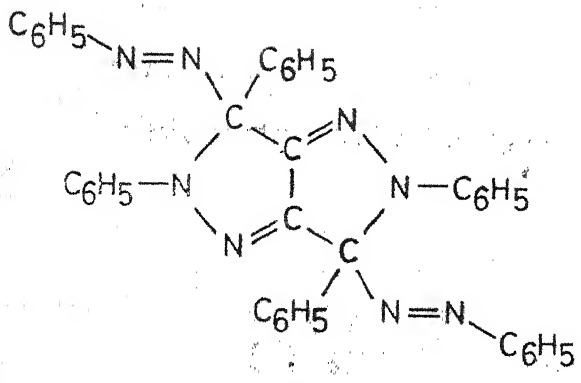
33 37 39 38 40 41

Scheme III·8 (Contd.)

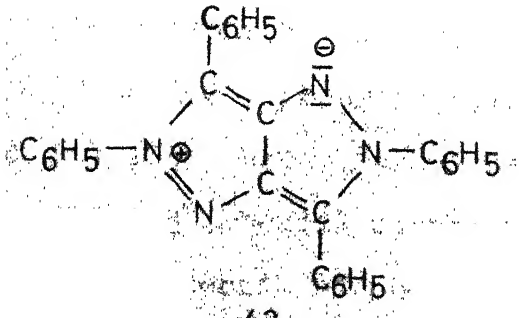


41





42



43

pentalene 43, on the other hand, may be occurring through the pseudoallylic radical intermediate 33, which undergoes dimerization to give the intermediate 37. This dimer 37 can undergo oxidative cyclization through several possible routes to the phenylazoalkane intermediate 42. Homolytic fragmentation of 42, involving the loss of phenylazo groups would result in the formation of 43 (Scheme III.8).

III.3 EXPERIMENTAL

All melting points are uncorrected and were taken on a Melt-Temp, melting point apparatus. The infrared spectra were recorded on a Perkin-Elmer, Model 137, infracord spectrometer and electronic spectra on a Beckmann DB-spectrophotometer. NMR traces were recorded on a Varian A-60 NMR spectrometer, using tetramethylsilane as an internal standard.

Starting Materials

Nickel peroxide (65 g) was prepared by the treatment of nickel sulfate (130 g) with a mixture of sodium hypochlorite (6% solution, 300 ml) and sodium hydroxide (42 g) as per a reported procedure.[18] Glyoxal bisphenylhydrazone,[19] mp 169-170°, methylglyoxal bisphenylhydrazone,[20] mp 145°, biacetyl bisphenylhydrazone,[3a] mp 245°, phenylglyoxal bisphenylhydrazone,[21] mp 152°, phenylmethylglyoxal bisphenylhydrazone,[22] mp 104-105°, benzylmethyl glyoxal bisphenylhydrazone,[22] mp 172-173°, benzil bisphenylhydrazone,[23] mp 236°, 4,4'-dimethoxybenzil bisphenylhydrazone,[24]

mp 197-198°, and acenaphthenequinone bisphenylhydrazone,[25] mp 219° were prepared from the corresponding 1,2-diketones with two equivalents of phenylhydrazine as per reported procedures.

4,4'-Dichlorobenzil bisphenylhydrazone (4d), which has not been reported in the literature, was prepared by treating a mixture of 4,4'-dichlorobenzil (1.4 g, 10 mmol) and phenylhydrazine (1.51 g, 14 mmol) in acetic acid (10 ml for 3 hr, on a water bath. The product (1.8 g) which separated out, on cooling the solution, was filtered and then recrystallized from ethanol to give 1.7 g (73%) of 4d, mp 192-193°.

Anal. Calcd for $C_{26}H_{20}N_4Cl_2$: C, 67.98; H, 4.36; N, 12.20. Found: C, 67.96; H, 4.07; N, 11.97.

The ir spectrum (KBr) of 4d showed an N-H band at 3250 cm^{-1} and C=N absorption band at 1600 cm^{-1}.

Uv spectrum λ max (Ethanol): 246 nm (ϵ ,41,000), 300 (18,000) and 356 (41,500).

Oxidation of Glyoxal Bisphenylhydrazone (4a)

A In Benzene at Room Temperature

A mixture of glyoxal bisphenylhydrazone (2 g, 8 mmol) and nickel peroxide (6 g) was stirred in benzene (150 ml) at room temperature for 3 hr. Removal of the inorganic material and the solvent gave 1.85 g (93%) of 1,2-bisphenylazoethylene, 6a, mp 143-144°(d). Recrystallization from ethanol gave a pure product melting at 149°(d). There was no depression in its melting point, when mixed with an authentic sample

of 6a.[3b]

B In Refluxing Benzene

In a repeat experiment, 2 g (8 mmol) of glyoxal bisphenylhydrazone and 6 g of nickel peroxide were refluxed in benzene (150 ml) for 4 hr. Work-up of the mixture in the usual manner and chromatography over alumina employing petroleum ether (bp 60-80°) gave 50 mg (4%) of biphenyl, mp 70° (mixture mp). Further elution of the column with benzene gave a product which on recrystallization from ethanol gave 1.48 g (75%) of 1,2-bisphenylazoethylene (6a), mp 149°(d) (mixture mp).

Oxidation of Benzil Bisphenylhydrazone (4b)

A In Benzene at Room Temperature

A mixture of benzil bisphenylhydrazone (2 g, 5.13 mmol) and nickel peroxide (4 g) was stirred in benzene at room temperature for 3 hr. Work-up of the mixture as in the earlier cases gave a solid which was filtered and washed with a mixture (2:1) of benzene and petroleum ether (bp 60-80°). Recrystallization of the solid from a mixture (1:1) of benzene and petroleum ether gave 1.2 g (60%) of 1,2-bisphenylazostilbene (6b), mp 179° (mixture mp).[5]

The mother liquor after removal of the solid product was chromatographed over alumina. Elution with petroleum ether gave 0.2 g (13%) of 2,4,6-triphenyl-1,2,3-triazole (8b), mp 124° (mixture mp). Further elution of the column with the same solvent gave an additional 0.2 g (11%) of 1,2-bis-

phenylazostilbene (6b), mp 179° (mixture mp).

B In Refluxing Benzene

In a repeat run, benzil bisphenylhydrazone (2 g, 5.13 mmol) and nickel peroxide (4 g) were refluxed in benzene (150 ml) for 3 hr. Work-up of the mixture as in the earlier cases gave a solid which was treated with a mixture (2:1) of petroleum ether and benzene. The insoluble material was filtered and the mother liquor was worked-up separately. The solid was recrystallized from a mixture (1:1) of benzene and petroleum ether to give 1.3 g (66%) of 1,2-bisphenylazostilbene (6b), mp 179° (mixture mp).

The mother liquor was chromatographed on alumina. Elution with petroleum ether gave a product which on recrystallization from petroleum ether gave 0.25 g (16%) of 2,4,5-triphenyl-1,2,3-triazole (8b), mp 124° (mixture mp). The mother liquor showed the presence of azobenzene on a tlc plate (silica gel).

Oxidation of 4,4'-Dimethoxybenzil Bisphenylhydrazone (4c)

Stirring a mixture of 4,4'-dimethoxybenzil bisphenylhydrazone (1.5 g, 3.3 mmol) and nickel peroxide (3.5 g) in benzene (125 ml) for 3 hr. at room temperature and work-up in the usual manner gave a product which was treated with a mixture (1:1) of petroleum ether and benzene. The insoluble portion was recrystallized from a mixture (1:1) of benzene and petroleum ether to give 0.45 g (31%) of 4,4'-dimethoxy-bisphenylazostilbene (6c), mp 175°.

Anal. Calcd for $C_{28}H_{24}N_2O_2$: C, 74.99; H, 5.36; N, 12.50. Found: C, 74.54; H, 5.27; N, 12.60.

The infrared spectrum (KBr) of 6c did not show any N-H band.

The uv spectrum ($CHCl_3$) of 6c showed the following absorption maxima: 272 nm (ϵ ,28,800), 320 (18,600), 332 (13,500) and 450 (5,000).

The mother liquor after the removal of the insoluble product was chromatographed over alumina. Elution with a mixture (1:1) of benzene and petroleum ether gave a solid material which was recrystallized from ethanol to give 0.25 g (21%) of 2-phenyl-4,5-dianisyl-1,2,3-triazole (8c), mp 133° (mixture mp).[2] Further elution of the column with benzene gave a solid which on recrystallization from a mixture of petroleum ether and benzene gave an additional yield of 0.25 g (17%) of (6c), mp 175° (mixture mp).

Oxidation of 4,4'-Dichlorobenzil Bisphenylhydrazone (4d)

A mixture of 4,4'-dichlorobenzil bisphenylhydrazone (1.5 g, 3.26 mmol) and nickel peroxide (3.5 g) in benzene (150 ml) was stirred at room temperature for 2½ hr. Removal of the inorganic material and of the solvent gave a solid which was recrystallized from a mixture (2:1) of benzene and petroleum ether to give 1.3 g (87%) of 4,4'-dichlorobisphenylazostilbene (6d), mp 205°.

Anal. Calcd for $C_{26}H_{18}N_4Cl_2$: C, 68.28; H, 3.94; N, 12.26. Found: C, 68.36; H, 4.05; N, 12.26.

The ir spectrum (KBr) of 6d did not show any N-H band.

The uv spectrum ($CHCl_3$) of 6d showed the following absorption maxima: 264 nm (ϵ ,20,500), 296 (18,000), 324 (14,400), 406 (18,400) and 480 (1,700).

Oxidation of Acenaphthenequinone Bisphenylhydrazone (4e)

A In Benzene at Room Temperature

A mixture of acenaphthenequinone bisphenylhydrazone (1 g, 2.84 mmol) and nickel peroxide (2.5 g) in benzene (175 ml) was stirred at room temperature for 1½ hr. Removal of the inorganic material and of the solvent gave 0.98 g of a solid which on recrystallization from a mixture (1:1) of benzene and alcohol gave 0.95 g (96%) of 1,2-bisphenylazoacenaphthalene (6e), mp 180°, as black shining needles.

Anal. Calcd for $C_{24}H_{16}N_4$: C, 80.00; H, 4.44; N, 15.55. Found: C, 80.00; H, 4.53; N, 15.60.

The ir spectrum (KBr) of 6e did not show any N-H band.

The uv spectrum (CH_2Cl_2) of 6e showed the following absorption maxima: 320 nm (ϵ ,26,700), 372 (28,900) and 472 (15,700).

B In Refluxing Benzene

A mixture of acenaphthenequinone bisphenylhydrazone (1 g, 2.84 mmol) and nickel peroxide (2.5 g) in 175 ml of benzene was refluxed for 3 hr. Work-up of the mixture as in the earlier cases gave a solid which was recrystallized

from a mixture (1:1) of benzene and alcohol to give 0.95 g (96%) of 1,2-bisphenylazoacenaphthalene (6e), mp 180° (mixture mp).

Oxidation of Methylglyoxal Bisphenylhydrazone (10a)

A In Benzene at Room Temperature

A solution of methylglyoxal bisphenylhydrazone (2 g, 8 mmol) in 150 ml of benzene and nickel peroxide (3.5 g) were stirred at room temperature for 4 hr. Work-up of the mixture in the usual manner gave a product, which on recrystallization from ethanol gave 1.8 g (90%) of 1,2-bisphenylazopropylene (12a) mp 106-107° (mixture mp).[3a]

B In Refluxing Benzene

A mixture of methylglyoxal bisphenylhydrazone (2 g, 8 mmol) and nickel peroxide (8 g) in 150 ml of benzene was refluxed for 6 hr. Work-up of the mixture gave a viscous liquid, which was chromatographed over alumina. Elution of the column with petroleum ether gave 40 mg (3%) of biphenyl, mp 170° (mixture mp). Further elution of the column with petroleum ether gave 0.9 g (45%) of 1,2-bisphenylazopropylene (12a), mp 106-107° (mixture mp), after recrystallization from ethanol. Subsequent elution of the column with a mixture (1:1) of petroleum ether and benzene gave 0.3 g (15%) 1-phenyl-4-phenylazopyrazole (16a), mp 126-127° (mixture mp),[26] after recrystallization from cyclohexane. A small amount (0.3 g, 15%) of the starting material, mp 145° (mixture mp) was also recovered from this run.

Oxidation of Biacetyl Bisphenylhydrazone (10b)

A In Benzene at Room Temperature

Treatment of biacetyl bisphenylhydrazone (2 g, 7 mmol) with nickel peroxide (6 g) in benzene (150 ml) for 4 hr. at room temperature and work-up of the mixture in the usual manner gave a product which after recrystallization from ethanol gave 1.7 g (85%) of 2,3-bisphenylazobut-2-ene (12b), mp 159°(d) (mixture mp).[4]

B In Refluxing Benzene

In a repeat run, 3 g (10.5 mmol) of biacetyl bisphenylhydrazone and 9 g of nickel peroxide in 150 ml of benzene were refluxed for 5 hr. Work-up of the mixture in the usual manner and chromatography over alumina, using petroleum ether as eluent, gave 0.1 g of biphenyl, mp and mmp 70°. Further elution of the column with a mixture (1:1) of petroleum ether and benzene gave 1.7 g of a crude product, which after recrystallization from cyclohexane gave 1.52 g (52%) of 1-phenyl-3-methyl-4-phenylazopyrazole (16b), mp 127°.

Anal. Calcd for $C_{16}H_{14}N_4$: C, 73.20; H, 5.30; N, 21.30. Found: C, 72.80; H, 5.50; N, 21.30.

The ir spectrum (KBr) of 16b did not show any N-H band.

The uv spectrum λ max (Ethanol): 220 nm (ϵ ,13,400), 340 (17,800) and 430 (1,150).

The nmr spectrum of 16b in $CDCl_3$ showed chemical shifts at 2.6 δ(3H, singlet) due to methyl protons, 7.6 δ (10H, multiplet) due to phenyl protons and 8.3 δ(1H, singlet)

due to the pyrazolyl proton.

Oxidation of Phenylmethylglyoxal Bisphenylhydrazone (10c)

A In Benzene at Room Temperature

A mixture of phenylmethylglyoxal bisphenylhydrazone (0.8 g, 2.4 mmol) and nickel peroxide (2.4 g) was stirred in benzene (125 ml) for 4 hr. at room temperature. Removal of the inorganic material and of the solvent gave a viscous material which was chromatographed over alumina. Elution with a mixture (1:1) of petroleum ether and benzene gave 0.6 g (76%) of 1,3-diphenyl-4-phenylazopyrazole, 16c, mp 113° (lit.[27] mp 113°), after recrystallization from cyclohexane.

B In Refluxing Benzene

In a repeat run, phenylmethylglyoxal bisphenylhydrazone (3 g, 9 mmol) and nickel peroxide (12 g) were refluxed in benzene (175 ml) for 4 hr. Work-up of the mixture as in the previous cases gave a viscous liquid which was chromatographed over alumina. Elution with petroleum ether gave 0.3 g (21%) of biphenyl, mp and mmp 70°. Further elution of the column with a mixture (1:1) of petroleum ether and benzene gave 2 g of a material, which on recrystallization from cyclohexane gave 1.7 g (58%) of 1,3-diphenyl-4-phenylazopyrazole (16c), mp 113° (mixture mp).

Oxidation of Benzylmethylglyoxal Bisphenylhydrazone (17)

A In Benzene at Room Temperature

A mixture of benzylmethylglyoxal bisphenylhydrazone

(0.8 g, 2.3 mmol) and nickel peroxide (2 g) was stirred in benzene (125 ml) at room temperature for 2 hr. Work-up of the mixture in the usual manner gave a red viscous liquid which was chromatographed on alumina. Elution of the column with a mixture (2:1) of petroleum ether and benzene gave a product, which was recrystallized from petroleum ether to give 0.15 g (19%) of 4-phenyl-3-phenylazo-3-buten-2-one phenylhydrazone (19), mp 124-125°.

Anal. Calcd for $C_{22}H_{20}N_4$: C, 77.65; H, 5.88; N, 16.47; Mol. wt., 340. Found: C, 77.76; H, 5.85; N, 16.15; Mol. wt., 340 (mass spectrometry).

The ir spectrum (KBr) of 19 showed absorption bands at 3350 cm^{-1} (N-H), 1600 cm^{-1} (C=N), and 1500 cm^{-1} (C=C).

The nmr spectrum of 19 in $CDCl_3$ showed a singlet at 2.17 δ (3H) due to the methyl protons, a multiplet centred around 7.23 δ (16H) due to the phenyl protons and a singlet at 7.85 δ (1H) due to the vinylic proton. The N-H proton appeared to be merged with the aromatic protons.

Further elution of the column with the same solvent mixture gave a product, which on recrystallization from ethanol gave 0.4 g (50%) of 1,5-diphenyl-3-methyl-4-phenylazopyrazole (22), mp 136° (lit.[28] mp 136°).

B In Refluxing Benzene

A solution of benzylmethylglyoxal bisphenylhydrazone (1.3 g, 3.8 mmol) in 175 ml of benzene was refluxed with 3.5 g of nickel peroxide for 2½ hr. Work-up of the mixture

as in the earlier cases gave a red viscous liquid which was chromatographed on alumina. Elution with petroleum ether gave 20 mg (3%) of biphenyl, mp and mmp 70°. Further elution of the column with a mixture (2:1) of petroleum ether and benzene gave 0.2 g of a red material, which on recrystallization from petroleum ether gave 0.19 g (14%) of 4-phenyl-3-phenylazo-3-buten-2-one phenylhydrazone (19), mp 124-125° (mixture mp). Subsequent elution with the same mixture gave 0.85 g (67%) of 1,5-diphenyl-3-methyl-4-phenylazopyrazole (22), mp 136° (mixture mp).

Elution of the column with benzene gave a yellow solid which on recrystallization from ethanol gave 40 mg (3%) of 1-phenyl-3-benzoyl-4-phenylazopyrazole (29), mp 152-153°.

Anal. Calcd for $C_{22}H_{16}N_4O$: C, 75.0; H, 4.54; N, 15.91; Mol. wt., 352. Found: C, 75.11; H, 4.70; N, 15.56; Mol. wt.,352 (mass spectrometry).

The ir spectrum (KBr) of 29 showed the C=O absorption at 1665 cm^{-1}.

The uv spectrum λmax (Ethanol): 256 nm (ϵ,21,700), 284 (17,200), 342 (13,400) and 424 (1,050).

Oxidation of 4-Phenyl-3-phenylazo-3-buten-2-one Phenylhydrazone (19) with Nickel Peroxide

A mixture of 19 (25 mg, 0.073 mmol) and nickel peroxide (50 mg) was stirred in benzene (25 ml) for 3 hr at room temperature. Work-up of the mixture in the usual manner gave a product which on recrystallization from ethanol gave

18 mg (72%) of 1,5-diphenyl-3-methyl-4-phenylazopyrazole, (22), mp 136° (mixture mp).

Oxidation of Phenylglyoxal Bisphenylhydrazone (31)

Phenylglyoxal bisphenylhydrazone (3 g, 9 mmol) and nickel peroxide (12 g) were refluxed in benzene (175 ml) for 4 hr. Removal of the inorganic material and the solvent gave a viscous liquid which was chromatographed over alumina. Elution with petroleum ether gave 0.3 g (20%) of biphenyl mp 70° (mixture mp). Further elution of the column with a mixture (3:1) of petroleum ether and benzene gave a semi-solid product, which on recrystallization from petroleum ether gave 0.4 g (19%) of 2,5-diphenyl-1,2,3-triazole (36), mp 52° (lit.[29] mp 52°).

Further elution of the column with benzene gave a viscous mass, which after repeated chromatography and recrystallization from a mixture of benzene and petroleum ether gave 0.35 g (18%) of 2,3,5,6-tetraphenyl-1,2,4,5-tetraazapentalene (43), mp 315°.

Anal. Calcd for $C_{28}H_{20}N_4$: C, 81.50; H, 4.80; N, 13.50; Mol. wt., 412. Found: C, 81.20; H, 4.70; N, 13.30; Mol. wt., 412 (mass spectrometry).

The ir spectrum (KBr) of 43 did not show any N-H band.

The uv spectrum (Ethanol) of 43 showed the following absorption maxima: 278 nm (ϵ, 31,200) and 386 (22,300).

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CHAPTER IV

OXIDATION OF BENZOYLHYDRAZONES OF ALDEHYDES, KETONES AND 1,2-DIKETONES WITH NICKEL PEROXIDE

IV.1 ABSTRACT

Benzaldehyde benzoylhydrazone on oxidation with nickel peroxide gives a mixture of 2,5-diphenyl-1,3,4-oxadiazole and nickel-bis-benzaldehyde benzoylhydrazone. Similarly, p-tolualdehyde benzoylhydrazone, o-methoxybenzaldehyde benzoylhydrazone and anisaldehyde benzoylhydrazone give the corresponding 1,3,4-oxadiazole derivatives and nickel complexes. Acetophenone benzoylhydrazone, on the other hand, gives a mixture of acetophenone and methylbenzylidene-α-dibenzoylamino-α-methylbenzylamine. Similarly, propiophenone benzoylhydrazone and benzophenone benzoylhydrazone give the corresponding ketones and Schiff's bases. Biacetyl bisbenzoylhydrazone and benzil bisbenzoylhydrazone on oxidation with nickel peroxide in chloroform give the corresponding enol-benzoates and nickel complexes. In contrast, phenylmethylglyoxal bisbenzoylhydrazone gives only the enol-benzoate under analogous conditions. Phenylglyoxal bisbenzoylhydrazone on oxidation with nickel peroxide gives a mixture of products consisting of 1-dibenzoylamino-4-phenyl-

1,2,3-triazole, 1-benzoylamino-4-phenyl-1,2,3-triazole and nickel-bis-phenyl-2-(5-phenyl-1,3,4-oxadiazolyl)-ketone benzoylhydrazone. Similarly, 4-methoxyphenylglyoxal bis-benzoylhydrazone gives a mixture of triazoles and the corresponding nickel complex.

IV.2 RESULTS AND DISCUSSION

In continuation of our work on the oxidation of bis-phenylhydrazones of 1,2-diketones, we have examined the oxidation of benzoylhydrazones of aldehydes, ketones and 1,2-diketones with nickel peroxide to study the nature of the products formed in these cases.

Aldehyde benzoylhydrazones have been oxidized by several reagents like alkaline potassium ferricyanide,[1] amyl nitrite,[1] chlorine[2] and iodine[1] and the major products in these oxidations have been characterized as 1,3,4-oxadiazole derivatives. In the present studies, we have examined the reaction of several aldehyde benzoylhydrazones with nickel peroxide. Benzaldehyde benzoylhydrazone (1a), for example, on treatment with nickel peroxide in refluxing chloroform gives a 30% yield of 2,5-diphenyl-1,3,4-oxadiazole (6a) and a 47% yield of a nickel complex, melting at 306-307° and identified as trans-nickel-bis-benzaldehyde benzoylhydrazone (7a). The structure of 7a has been established on the basis of elemental analysis and spectral data. The ir spectrum of 7a does not show the presence of either N-H or C=O bands but shows the presence of a C=N band at 1625 cm^{-1}. Magnetic moment measurements indicates that the nickel complex is diamagnetic and has a square planar configuration

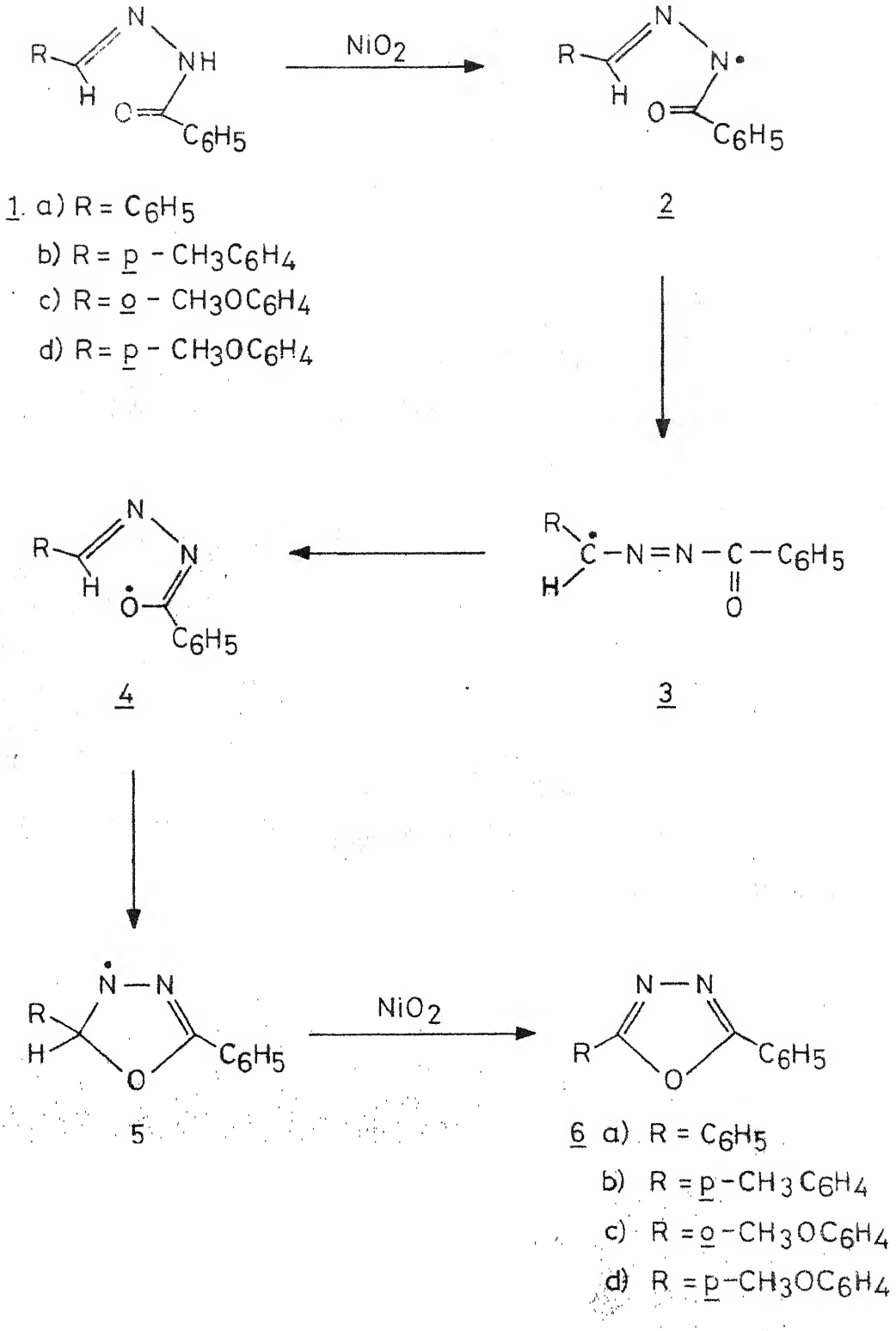
The formation of both 6a and 7a in the oxidation of 1a can be explained in terms of the pathway shown in Scheme IV.1. In this scheme, we assume that nickel peroxide abstracts a hydrogen atom from benzaldehyde benzoylhydrazone (1a) giving rise to a radical intermediate 2 which can isomerize to 3 or 4. The radical intermediate 4 can undergo an intramolecular cyclization to 5, which on further loss of a hydrogen atom will lead to the oxadiazole 6a.

The actual mode of formation of 7a is not very clear. A probable route would involve the reaction of the radical intermediate 4 with nickel hydroxide, a possible constituent of the oxide that is used for oxidation. Alternatively, an ionic pathway could also be suggested for the formation of 7a.

Similarly, the oxidation of p-tolualdehyde benzoylhydrazone (1b), o-methoxybenzaldehyde benzoylhydrazone (1c) and anisaldehyde benzoylhydrazone (1d) with nickel peroxide in chloroform give the corresponding 1,3,4-oxadiazole derivatives 6b-d in yields ranging between 20-35% and the nickel complexes 7b-d in 23-41% yields. In the case of o-methoxybenzaldehyde benzoylhydrazone, however, in addition to the oxadiazole derivative 6c and the nickel complex 7c, a 20% yield of o-methoxybenzaldehyde (9c) is also formed, which is isolated through its 2,4-dinitrophenylhydrazine derivative. The formation of 9c in this reaction may be explained through the hydroxy intermediate 8c formed from 3, which can subsequently undergo oxidative fragmentation as shown in Scheme IV.1.

The oxidation of only very few ketone benzoylhydrazones

Scheme IV.1



1. a) R = C_6H_5
   b) R = p - $CH_3C_6H_4$
   c) R = o - $CH_3OC_6H_4$
   d) R = p - $CH_3OC_6H_4$

2

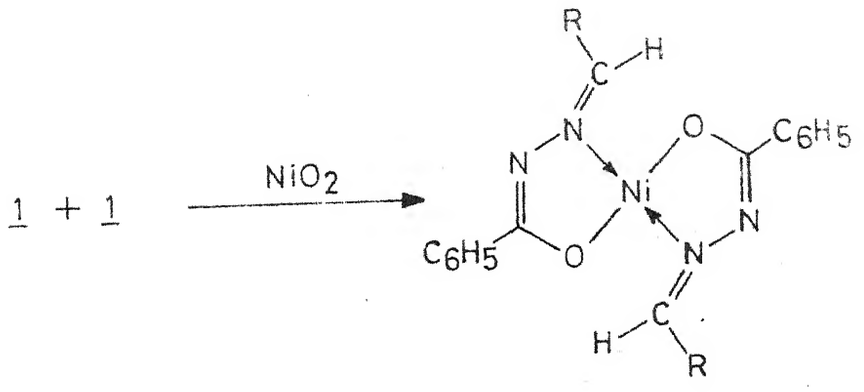
3

4

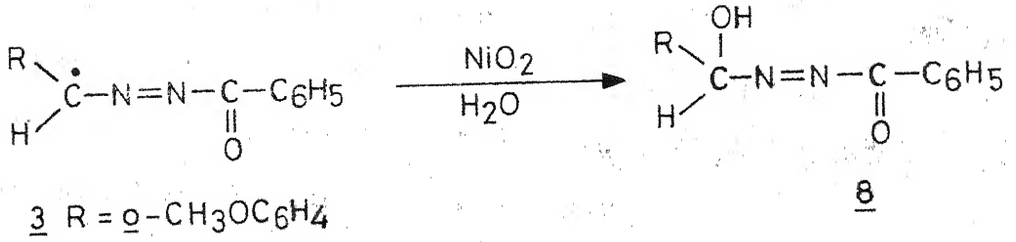
5

6 a) R = C_6H_5
   b) R = p-$CH_3C_6H_4$
   c) R = o-$CH_3OC_6H_4$
   d) R = p-$CH_3OC_6H_4$

Scheme IV·1 (Contd.)



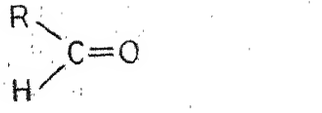
7 a) R = C_6H_5
b) R = p-$CH_3C_6H_4$
c) R = o-$CH_3OC_6H_4$
d) R = p-$CH_3OC_6H_4$



3 R = o-$CH_3OC_6H_4$

8

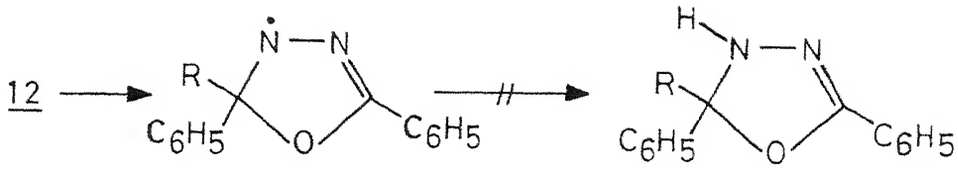
NiO_2



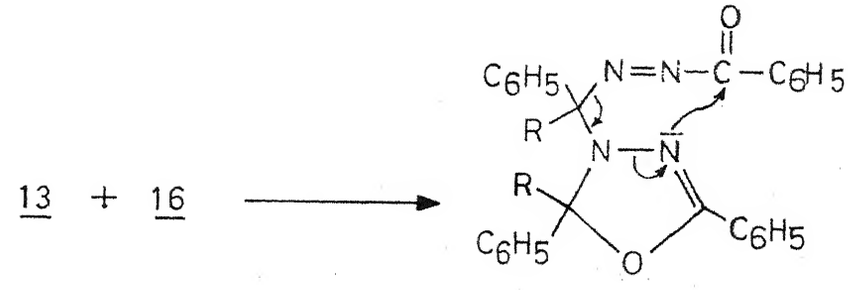
9 R = o-$CH_3OC_6H_4$

has been reported in the literature. The mercury complex of benzophenone benzoylhydrazone, for example, has been oxidised with iodine in ether, to give 2,2,5-triphenyl-3-benzoyl-2,3-dihydro-1,3,4-oxadiazole.[1] In the present studies, we have examined the oxidation of a few ketone benzoylhydrazones with nickel peroxide with a view to studying the nature of the products formed in these reactions. Acetophenone benzoylhydrazone (10a), for example, on treatment with nickel peroxide in refluxing benzene, gives a 36% yield of acetophenone (15a), identified through its 2,4-dinitrophenylhydrazone. In addition, a 11% yield of a colourless solid, mp 249-250° and analyzing for $C_{30}H_{26}N_2O_2$ has also been isolated. The structure of this product has been assigned as methylbenzylidene-α- dibenzoylamino-α-methylbenzylamine (20a), on the basis of spectral data and chemical evidences (Scheme IV.2). The ir spectrum of 20a shows the presence of two C=O groups at 1665 and 1660 cm^{-1}, respectively and a C=N group at 1640 cm^{-1}. The uv spectrum of 20a shows absorption bands at 230 nm (ϵ, 17,900), 280 (14,000) and 292 (12,400) similar to the uv characteristics of a mixture of methylbenzylidene-α-methylbenzylamine[3] and dibenzamide.[4] The nmr spectrum of 20a in deuterochloroform (Figure IV.1) shows chemical shifts at 1.73 δ (3H, singlet), 1.87 δ (3H, singlet) and between 7.0-8.2 δ (20H, multiplet). The appearance of the methyl groups as two separate signals at 1.73 δ and 1.87 δ indicate that they are magnetically non-equivalent. Treatment of 20a with 2,4-dinitrophenylhydrazine did not give rise to any 2,4-dinitrophenylhydrazone derivative, thereby indicating the

Scheme IV · 2 (Contd.)

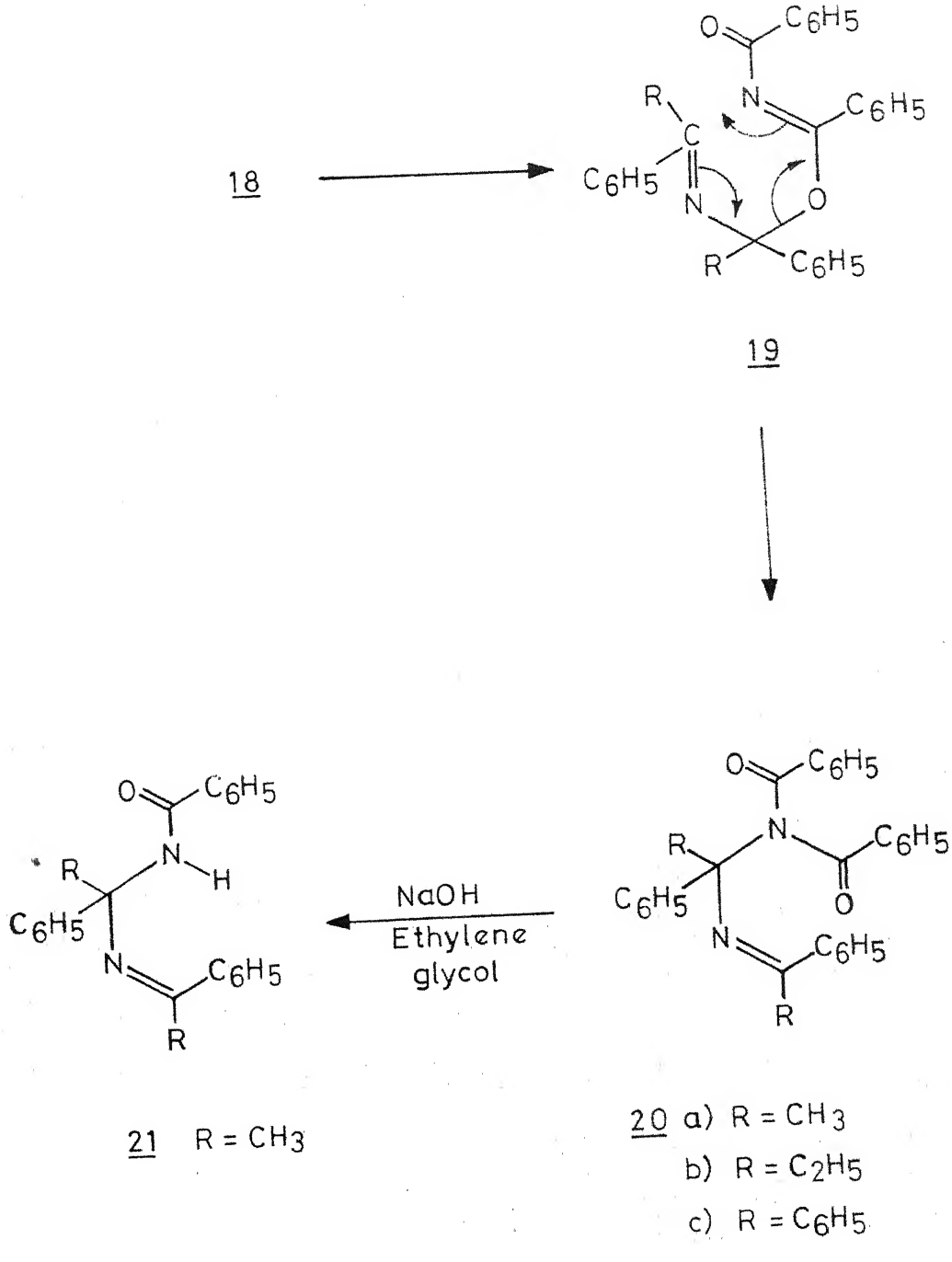


16 17



18

Scheme IV·2 (Contd.)



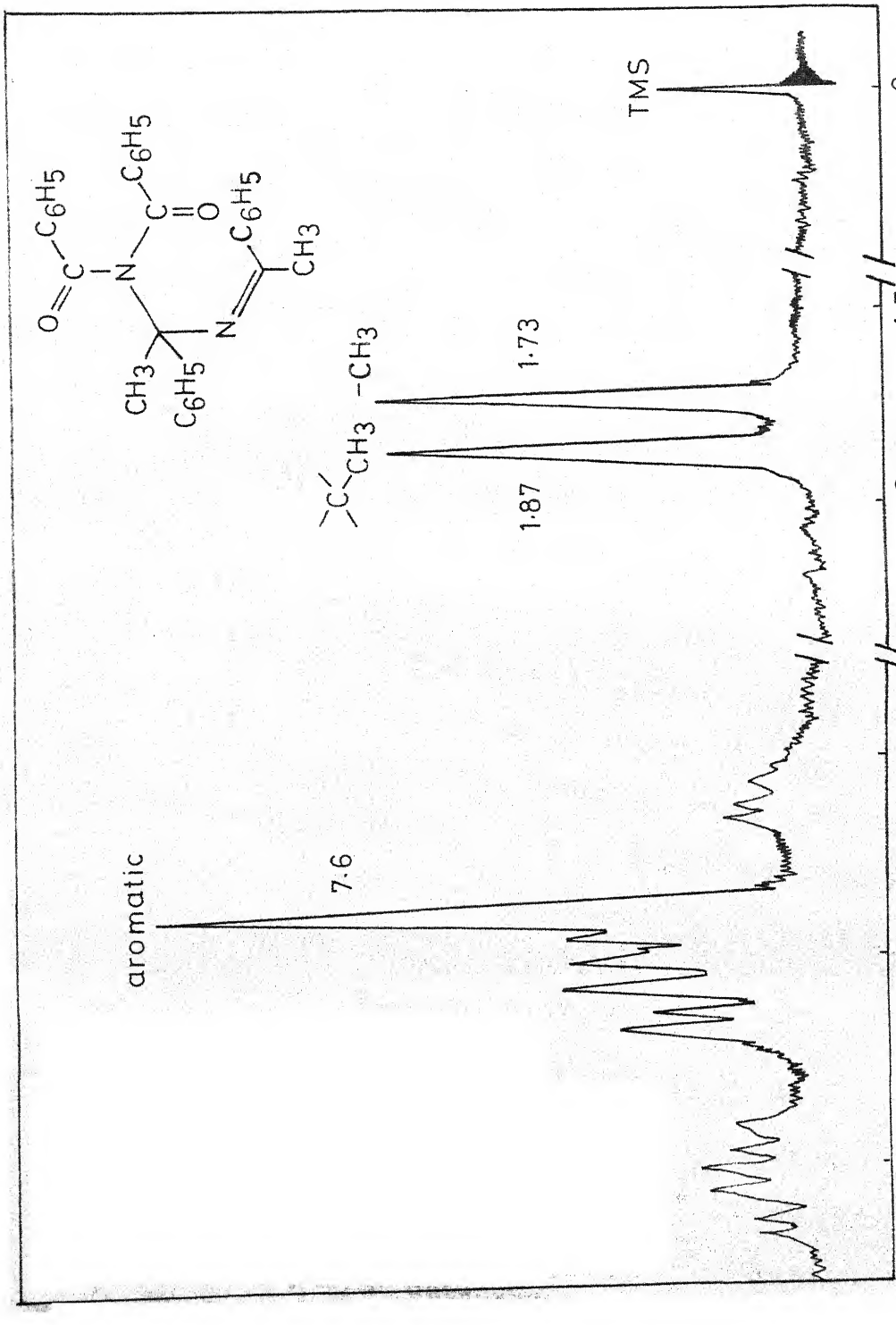


Fig. IV.1 NMR spectrum of methylbenzylidene-(C)-dibenzoyl-amino-α-methylbenzylamine (20a)

absence of a keto carbonyl group.

Further evidence concerning the structure 20a has been derived from its mass spectral data. The mass spectrum of 20a (Figure IV.2) shows the molecular ion peak at m/e 446. Other peaks are observed at m/e 341, 326, 311, 223, 208, 194, 179, 118, 105 and 77 which may be due to some of the fragments shown in Scheme IV.3. The species at m/e 341 is formulated as the ion corresponding to 20aa, formed by the loss of a benzoyl group from the molecular ion. Successive loss of two methyl groups from 20aa leads to the ions 20ab (m/e 326) and 20ac (m/e 311), respectively. The peak at m/e 223 has been assigned to 20ad, formed by the loss of acetophenoneimine from 20ac. Similarly, the loss of benzonitrile from 20ac leads to the ion 20ae at m/e 208 which is also formed from 20ad by the loss of a methyl group. Loss of a benzoyl group from 20ad leads to the fragment 20af at m/e 118. The fragment at m/e 105, corresponding to 20ag is formed by the loss of a second molecule of benzonitrile from 20ae. Loss of carbon monoxide from 20ag leads to the fragment 20ah at m/e 77.

Additional evidence concerning the structure of 20a is derived from degradative studies. Alkaline hydrolysis of 20a by refluxing it with sodium hydroxide in ethylene glycol for 8 hr gives a solid, melting at 164-165° and identified as methylbenzylidene-α-benzoylamino-α-methylbenzylamine (21), on the basis of analytical data and spectral evidences. Compound 21 analyses for $C_{23}H_{22}N_2O$ and its molecular weight is found to be 342 (mass spectrometry). Its ir spectrum shows an N-H

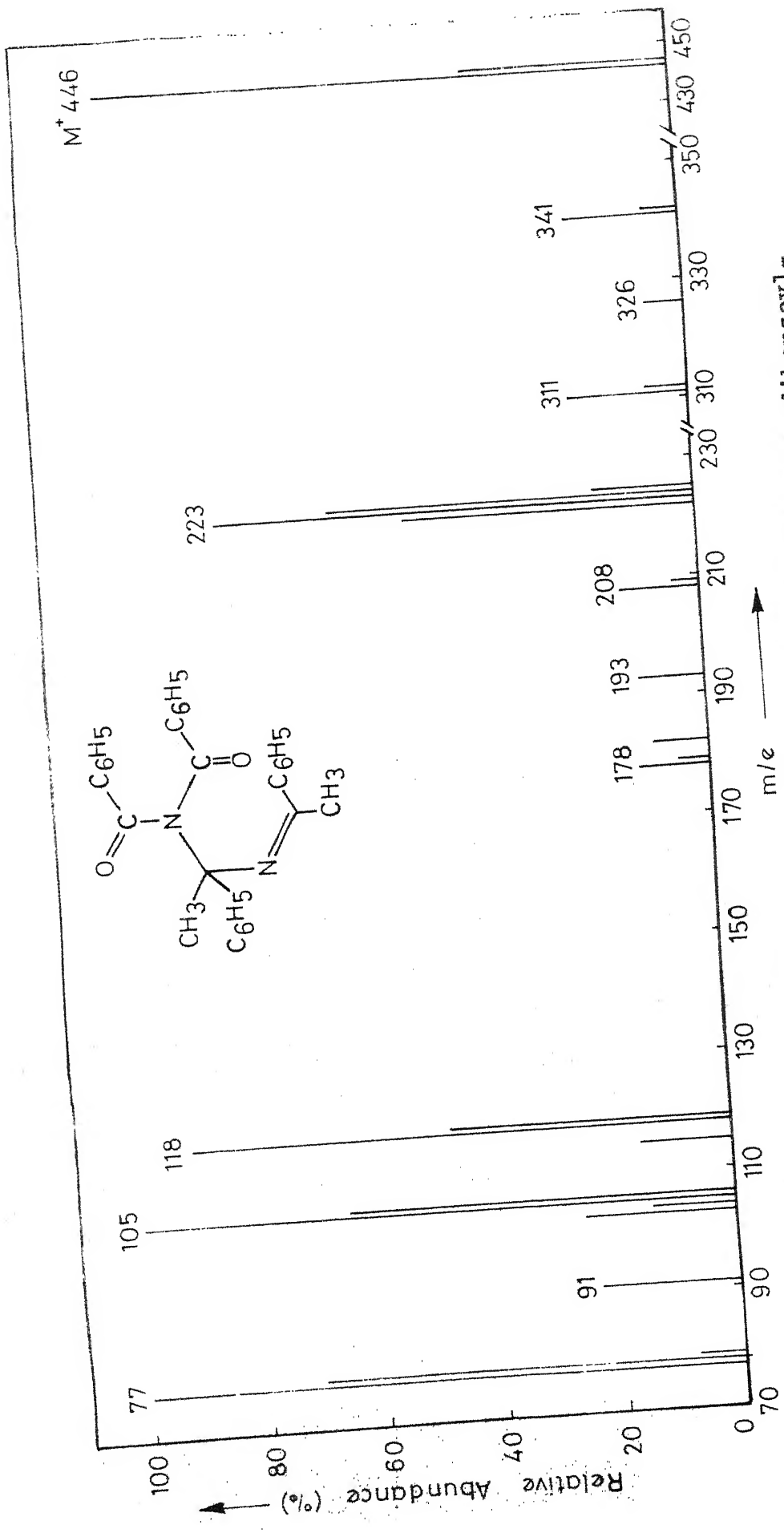
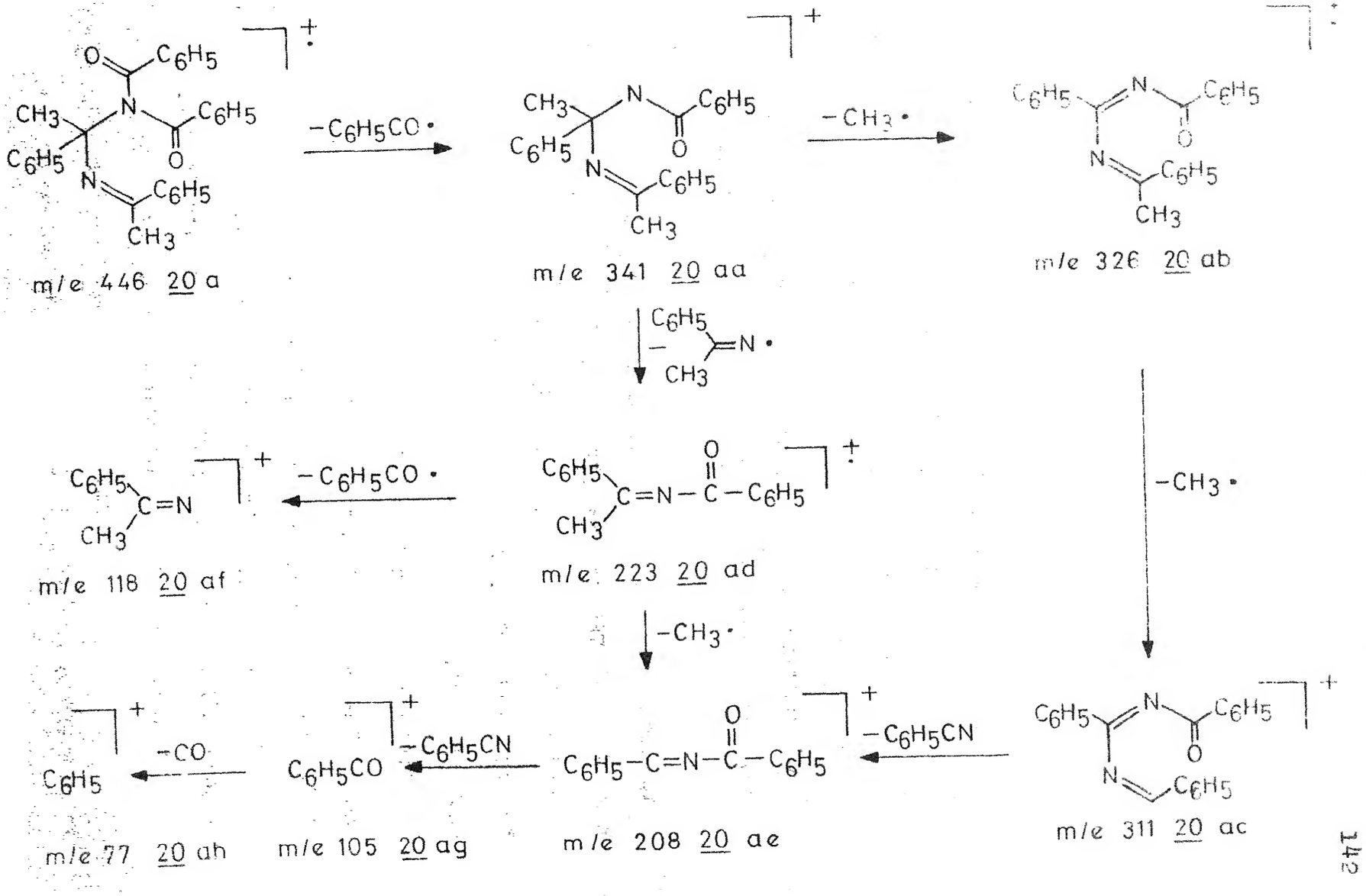


Fig.IV.2. Mass spectrum of methylbenzylidene-α-dibenzoyl-amino-α-methylbenzylamine (20a)

Scheme IV·3


m/e 446 20 a
m/e 341 20 aa
m/e 326 20 ab
m/e 311 20 ac
m/e 223 20 ad
m/e 208 20 ae
m/e 118 20 af
m/e 105 20 ag
m/e 77 20 ah
-C6H5CO·
-CH3·
-C6H5CN
-CO

absorption band at 3200 cm^{-1} and an amide carbonyl band at 1645 cm^{-1}. The uv spectrum of 21 is characterized by the presence of an absorption maximum at 286 nm (€ ,11,700).

Further confirmation of the structure of 21 is derived from its mass spectral data. The mass spectrum (Figure IV.3) of 21 showed the molecular ion peak at m/e 342. Other peaks are observed at m/e 237, 224, 208, 193, 180, 161, 145, 122, 119, 105 and 77, which could be assigned to some of the fragments shown in Scheme IV.4. The species at m/e 327 is formulated as the ion corresponding to 21a formed by the loss of a methyl group from the molecular ion. Further loss of a molecule of benzonitrile from 21a would lead to the ion 21b at m/e 224 which is the base peak in the spectrum. Another mode of fragmentation of the molecular ion is by the loss of a benzoyl group leading to the ion 21c at m/e 237. Successive loss of methyl and phenyl groups from 21c would lead to ions 21d and 21e at m/e 222 and 145, respectively. Further loss of a CN group from 21c would lead to the ion 21f at m/e 119. The same ion can also be formed by the loss of a benzoyl group from 21b. The peak at m/e 209 is assigned to the fragment 21g formed by the loss of a methyl group from 21b, which can then lose a proton giving rise to the fragment 21h at m/e 208. Loss of a molecule of carbon monoxide from 21h leads to the fragment 21i at m/e 180. The peaks at m/e 105 and 77 have been assigned to fragments 21j and 21ak, respectively.

The formation of both 15a and 20a in the oxidation of acetophenone benzoylhydrazone (10a) can be rationalized in

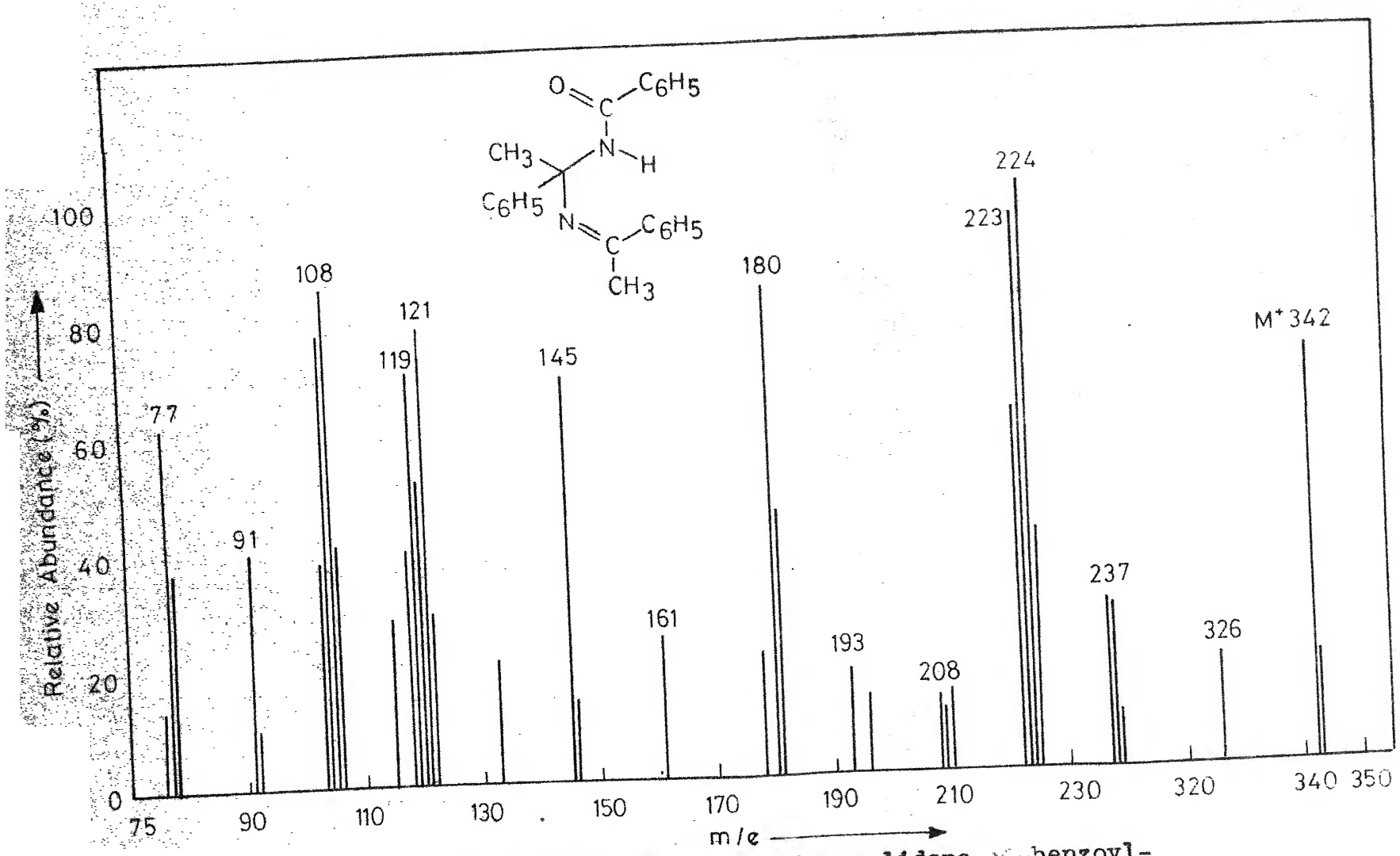
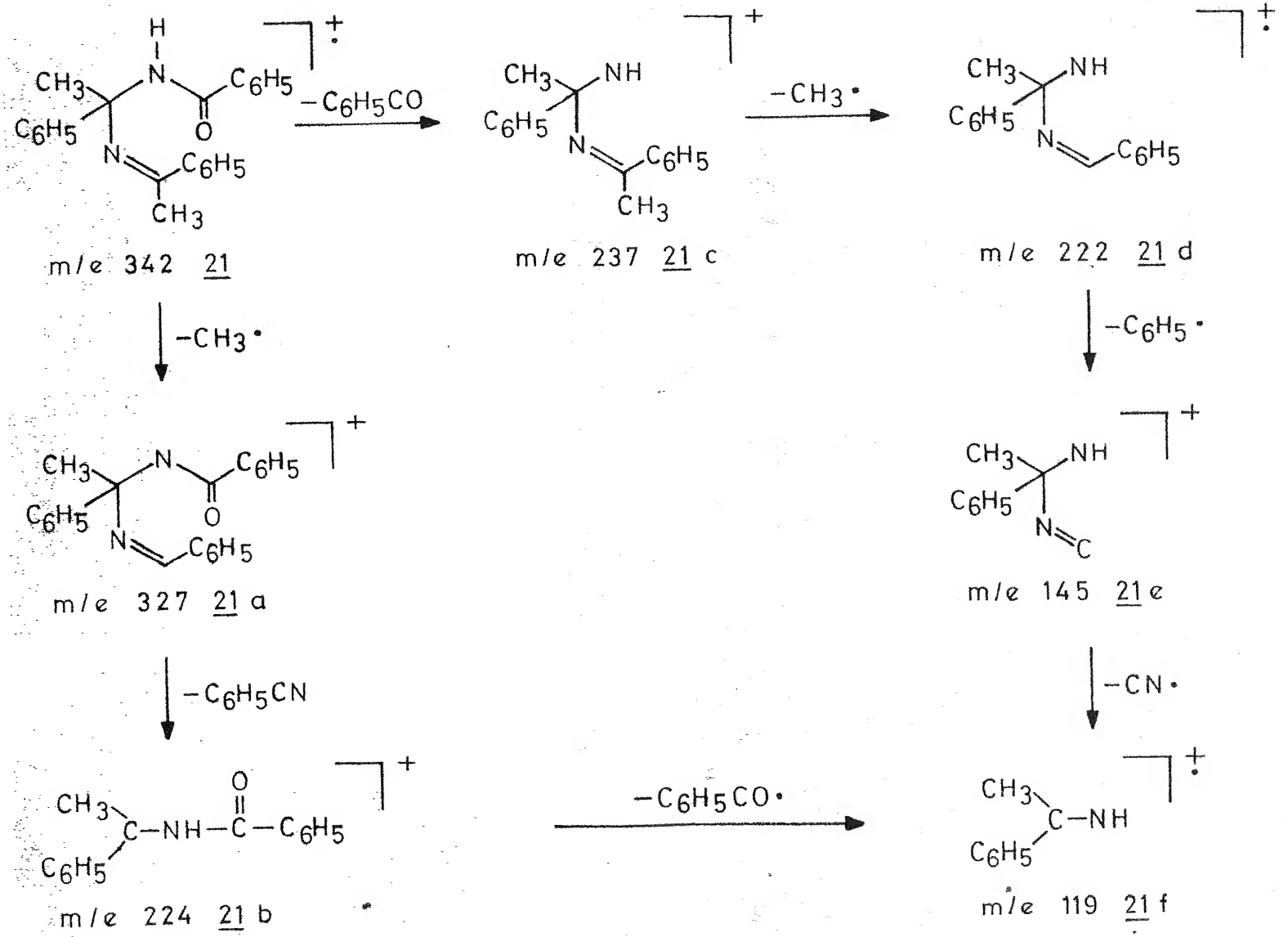
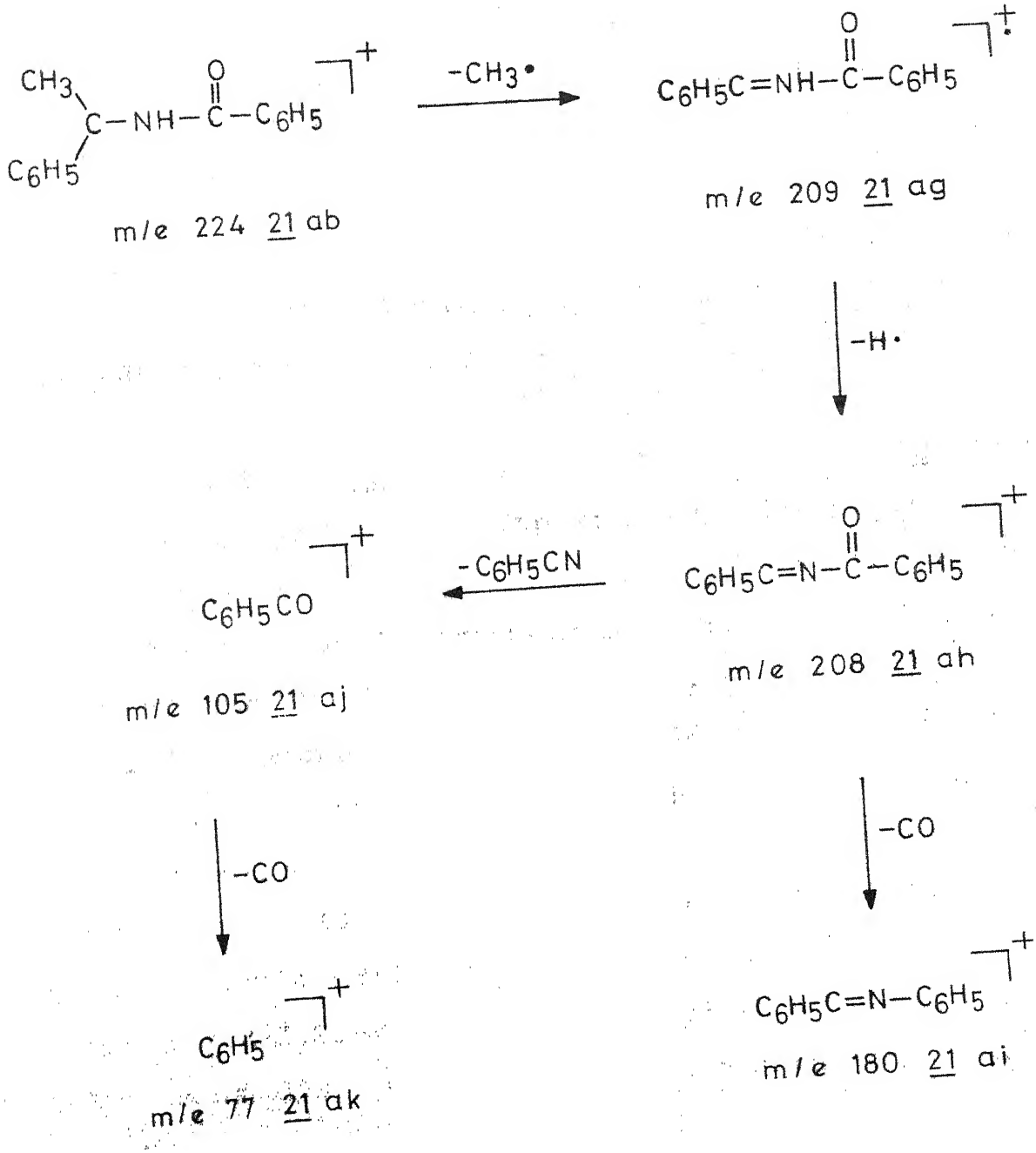


Fig.IV.3 Mass spectrum of methylbenzylidene-α'-benzoyl-amino-α-methylbenzylamine (21)

Scheme IV·4


m/e 342 21
m/e 237 21 c
m/e 222 21 d
m/e 327 21 a
m/e 145 21 e
m/e 224 21 b
m/e 119 21 f
-C6H5CO
-CH3·
-C6H5CN
-C6H5·
-CN·
-C6H5CO·

Scheme IV·4 (Contd.)



terms of a reaction mechanism shown in Scheme IV.2. In this scheme, we assume that the initial removal of a hydrogen atom from 10a by nickel peroxide can give rise to the radical intermediate 11 or one of its isomeric forms 12 or 13. Hydroxylation of the radical intermediate 13, followed by oxidative fragmentation in presence of nickel peroxide leads to the formation of acetophenone (15a). Another possible mode of reaction is the cyclization of the radical intermediate 12 giving rise to a new radical intermediate 16 which can then abstract a hydrogen atom from the solvent giving rise to the 2,3-dihydro-1,3,4-oxadiazole derivative 17. Interestingly enough this mode of reaction has not been observed under these conditions. On the other hand, a coupling reaction of the radical intermediates 13 and 16 would lead to the intermediate 18 which can then loose a molecule of nitrogen giving rise to 20a through the intermediate 19.

1,2-Diketone bisbenzoylhydrazones have been oxidized by several reagents like alkaline potassium ferricyanide,[5-10] a mixture of mercuric oxide and iodine,[7-9] silver oxide[8] and iodine.[1] It has been observed that the products formed in these reactions vary considerably with the nature of the oxidizing agent. Glyoxal bisbenzoylhydrazone, for example, on oxidation with alkaline potassium ferricyanide[6] gives a 2-benzoylamino-1,2,3-triazole, whereas 5,5'-diphenyl-2,2'-bis 1,3,4-oxadiazolyl is obtained when the mercury complex of glyoxal bisbenzoylhydrazone is oxidized with iodine.[1] Similarly, the oxidation of biacetyl bisbenzoylhydrazone[7] and

benzil bisbenzoylhydrazone[7] with alkaline potassium ferricyanide has been reported to give 1-benzoyloxybenzylideneamino-4,5-dimethyl-1,2,3-triazole and 1-benzoyloxybenzylideneamino-4,5-diphenyl-1,2,3-triazole, respectively. Considerable controversy exists in the literature concerning the structure of the oxidation products of 1,2-diketone bisbenzoylhydrazones. It has been assumed earlier that these oxidation products are essentially dihydro-1,2,3,4-tetrazine derivatives.[1,5,6,9] Petersen and Heitzer,[12] on the other hand, have suggested a mesoionic structure for the oxidation product obtained from biacetyl bisbenzoylhydrazone. However, recent studies[13,14] have shown that the oxidation products of 1,2-diketone bisbenzoylhydrazones are correctly represented as triazole derivatives containing enol-benzoate side chains. It has been reported that the oxidation of biacetyl bismesitoylhydrazone with either a mixture of mercuric oxide and iodine or alkaline potassium ferricyanide proceeds with oxidative fragmentation leading to the formation of acetonitrile and azodimesitoyl.[8] In contrast, the oxidation of benzil bismesitoylhydrazone with mercuric oxide and iodine gives 1-mesitoylamino-4,5-diphenyl-1,2,3-triazole.[8] It has been reported that the oxidation of benzil bismesitoylhydrazone with silver oxide in ether gives rise to disilver salt which on treatment with iodine in carbon disulfide gives 1-amino-4,5-diphenyl-1,2,3-triazole. However, the formation of the unstable bisbenzoylazostilbene is observed during shorter reaction periods and at lower temperatures.[8]

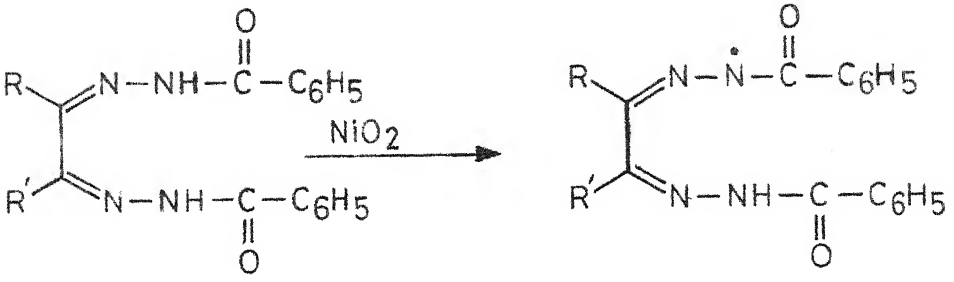
In the present investigation, we find that the oxidation

of biacetyl bisbenzoylhydrazone (22a) with nickel peroxide in refluxing chloroform gives rise to a 7% yield of 1-α-benzoyloxybenzylideneamino-4,5-dimethyl-1,2,3-triazole (26a) and a 24% yield of nickel-biacetyl bisbenzoylhydrazone (27a) (Scheme IV.5). Similarly, the oxidation of benzil bisbenzoylhydrazone (22b) gives a 26% yield of the enol-benzoate 26b and a 22% yield of the nickel complex 27b. In contrast, the oxidation of phenylmethylglyoxal bisbenzoylhydrazone (22c) gives only the enol-benzoate 26c. No nickel complex could be isolated from this reaction.

The formation of the enol-benzoates 26a-c in the oxidation of the bisbenzoylhydrazones of biacetyl, benzil and phenyl methylglyoxal can be rationalized in terms of the reaction sequences shown in Scheme IV.5. In this scheme, we assume that nickel peroxide abstracts a proton from 22 giving rise to the radical intermediate 23 which on further oxidation gives rise to the bisazobenzoylolefin 24. The bisazolefin 24 can, through the zwitterionic intermediate 25, rearrange to the enol-benzoate 26. The exact mode of formation of the nickel complexes 27a,b in these oxidations is not very clear. They could arise through an analogous pathway indicated for the formation of the nickel complexes from aldehyde benzoylhydrazones 1a-d.

Oxidation of phenylglyoxal bisbenzoylhydrazone (28a) with nickel peroxide in refluxing chloroform gives a mixture of products consisting of 1-dibenzoylamino-4-phenyl-1,2,3-triazole (33a) and 1-benzoylamino-4-phenyl-1,2,3-triazole (34a). In addition, a pink coloured nickel complex, melting at 321-322°

Scheme IV·5

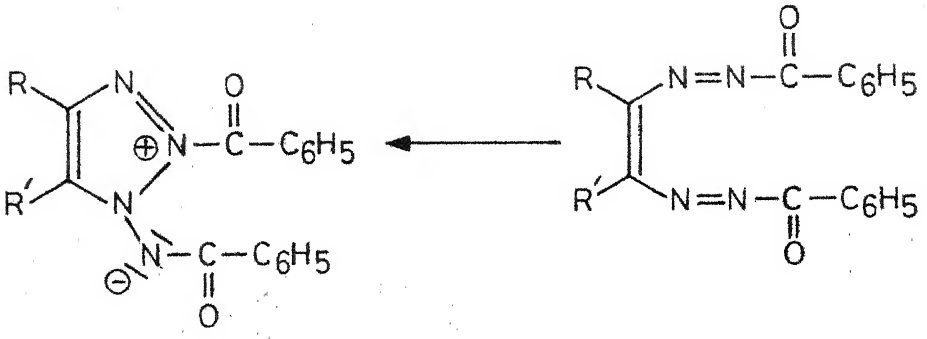


22 a) $R = R' = CH_3$

b) $R = R' = C_6H_5$

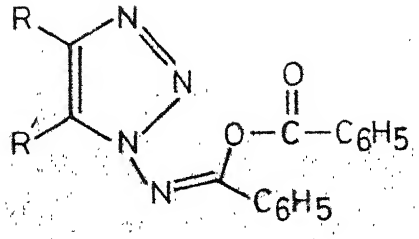
c) $R = C_6H_5$, $R' = CH_3$

23



25

24

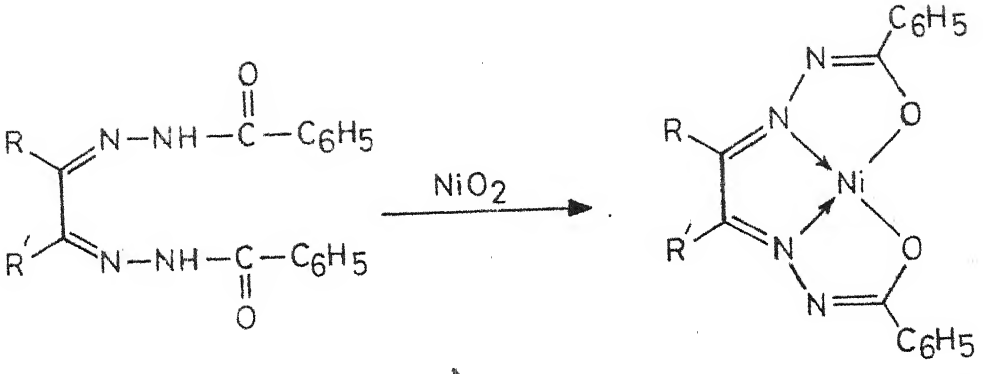


26 a) $R = R' = CH_3$

b) $R = R' = C_6H_5$

c) $R = C_6H_5$, $R' = CH_3$

Scheme IV·5 (Contd.)

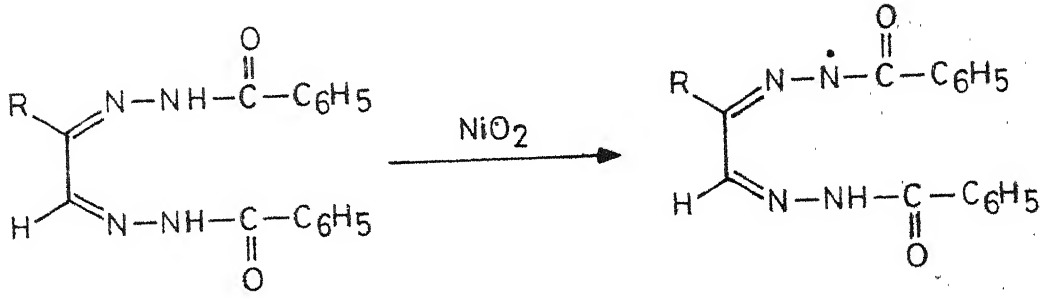


22 a,b

27 a) R = R′ = CH_3

b) R = R′ = C_6H_5

Scheme IV·6

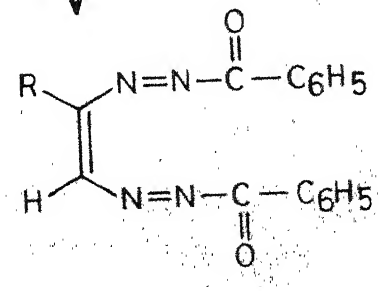


28. a) R = C_6H_5

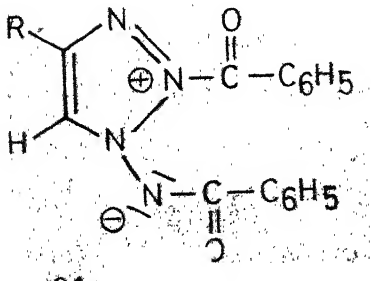
b) R = p-$CH_3OC_6H_4$

29

NiO_2

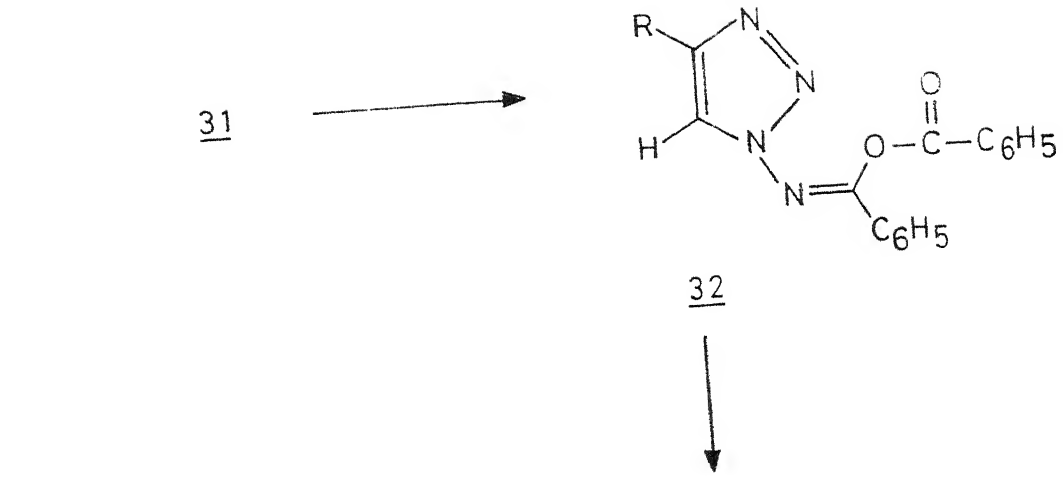


30

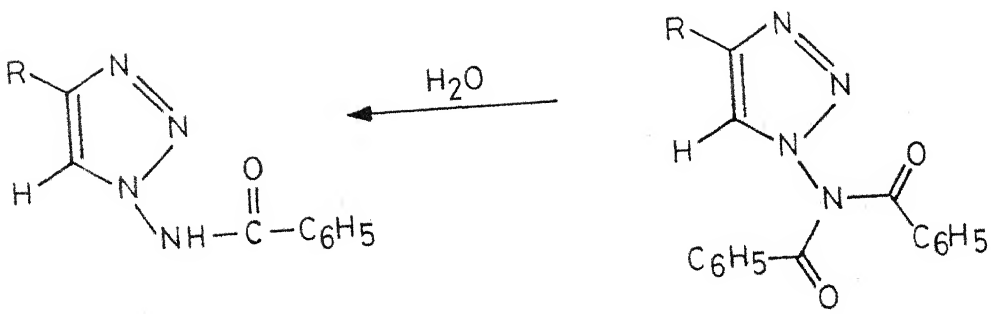


31

Scheme IV·6 (Contd.)



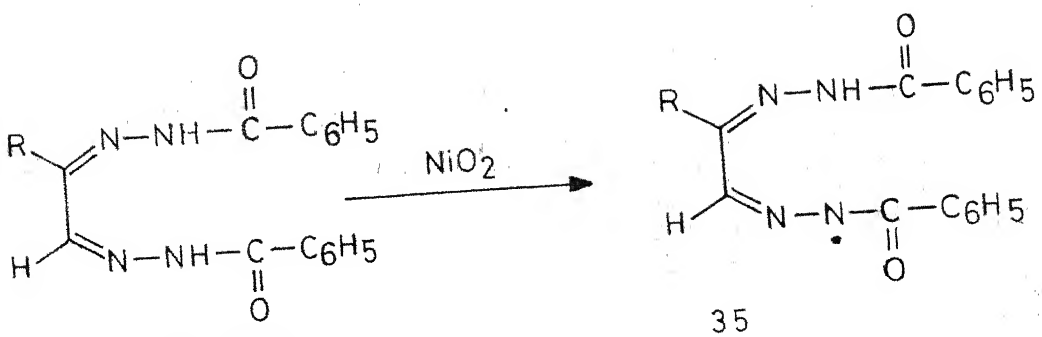
31 → 32



33 a,b → (H$_2$O) → 34

34 a) R = C_6H_5

b) R = p-$CH_3OC_6H_4$

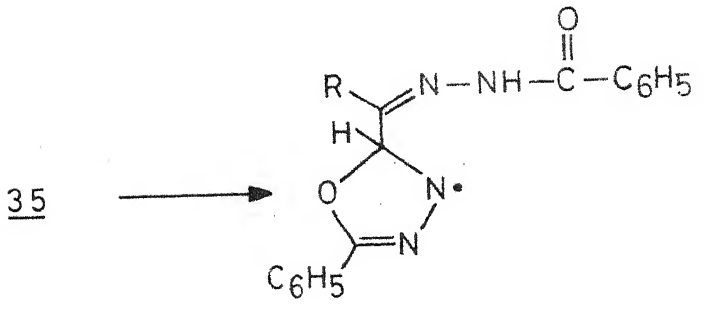


28 → (NiO_2) → 35

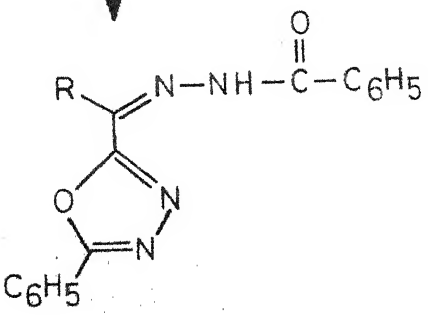
28 a) R = C_6H_5

b) R = p-$CH_3OC_6H_4$

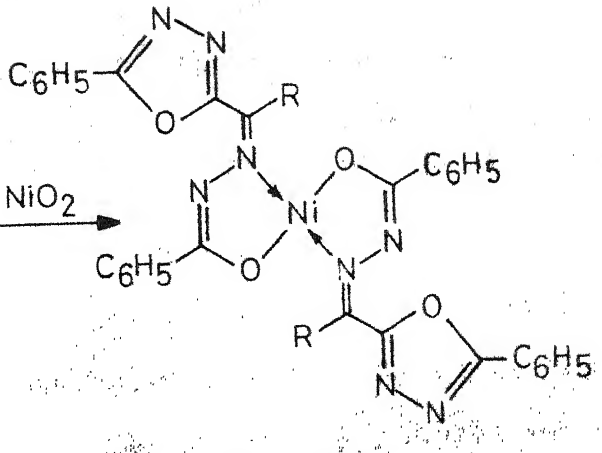
Scheme IV·6 (Contd.)



35 → 36



36 → (NiO2) → 37



37 + 37 → (NiO2) → 38 a) R = C6H5
b) R = p-CH3OC6H4

and analyzing for $C_{44}H_{30}N_8O_4Ni$ is also isolated from this reaction (Scheme IV.6). The ir spectrum of this complex does not show the presence of either NH or C=O groups. The uv spectrum of the product in chloroform shows two intense absorption maxima at 288 nm (ϵ ,33,600) and 426 (87,900). Magnetic moment measurement indicates that the complex is diamagnetic and hence has a square planar configuration. On the basis of these evidences, we have assigned structure 38a representing nickel-bis-phenyl-2-(5-phenyl-1,3,4-oxadiazolyl)-ketone benzoylhydrazone for this product. Similarly, the oxidation of 4-methoxyphenylglyoxal bisbenzoylhydrazone with nickel peroxide gives a 7% yield of 1-dibenzoylamino-4-(4-methoxyphenyl)-1,2,3-triazole (33b), a 9% yield of 1-benzoylamino-4-(4-methoxyphenyl)-1,2,3-triazole (34b) and a 6% yield of the nickel complex 38b.

The formation of the various products such as 33, 34 and 38 in the oxidation of phenylglyoxal bisbenzoylhydrazone (28a) and 4-methoxyphenylglyoxal bisbenzoylhydrazone (28b) may be rationalized in terms of the reaction sequences shown in Scheme IV.6. In this scheme, we assume that the initial oxidation product of 28 is the radical intermediate 29 which on further oxidation goes to the bisbenzoylazoolefin 30. Intramolecular cyclization of 30 leads to the zwitterionic intermediate 31 which subsequently rearranges to the enol-benzoate 32 and finally to the dibenzoylamino triazole 33. The formation of the 1-benzoylamino-1,2,3-triazole derivative 34 may be rationalized in terms of the hydrolysis of the

dibenzoyl derivative 33, under the reaction conditions. Another mode of oxidation of 28 is through the radical intermediate 35, which then cyclizes to give the intermediate 36. Subsequent oxidation of 36 would result in the formation of 1,3,4-oxadiazolyl ketone benzoylhydrazone 37. Two molecules of 37 can later react with nickel peroxide giving rise to the nickel complex 38.

IV.3 EXPERIMENTAL

Magnetic moment measurements were carried out on a Gouy balance by the standard procedure.

Starting Materials

Benzaldehyde benzoylhydrazone, mp 204-205°,[15] p-tolualdehyde benzoylhydrazone, mp 155°,[1] o-methoxybenzaldehyde benzoylhydrazone, mp 179°,[16] anisaldehyde benzoylhydrazone, mp 147°,[16] acetophenone benzoylhydrazone, mp 153°,[15] benzophenone benzoylhydrazone, mp 116-117°,[1] biacetyl bisbenzoylhydrazone, mp 286°,[6] phenylglyoxal bisbenzoylhydrazone, 240-241°,[14] and benzil bisbenzoylhydrazone, mp 206°,[15] were prepared as per reported procedures.

Propiophenone benzoylhydrazone (10b) was prepared by heating a mixture of propiophenone (2.68 g, 20 mmol) and benzhydrazide (2.72 g, 20 mmol) in an oil bath, around 125°, for 10 hr. The solid product was filtered off and recrystallized from ethanol to give 4.5 g (89%) of propiophenone benzoylhydrazone (10b), mp 155°.

Anal. Calcd for $C_{16}H_{16}N_2O$: C, 76.19; H, 6.35; N, 11.11

Found: C, 76.25; H, 6.41; N, 10.94.

The ir spectrum (KBr) of 10b showed the presence of an amide C=O band at 1660 cm^{-1}.

The uv spectrum (ethanol) of 10b showed an absorption maximum at 286 nm (ϵ ,24,700).

4-Methoxyphenylglyoxal bisbenzoylhydrazone (28b) was prepared by heating a mixture of 4-methoxyphenylglyoxal (0.82 g, 5.0 mmol) and benzhydrazide (1.53 g, 11.3 mmol) in ethanol (20 ml) containing acetic acid (1 ml) for 1 hr on a water-bath. The solid which separated out on cooling was filtered and then recrystallized from a mixture (1:1) of ethanol and benzene to give 1.7 g (85%) of 28b, mp 261-262°.

Anal. Calcd for $C_{23}H_{20}N_4O_3$: C, 69.00; H, 5.00; N, 14.00; Found: C, 69.33; H, 4.89; N, 13.68.

The ir spectrum (KBr) of 28b showed an amide C=O band at 1650 cm^{-1}.

The uv spectrum (ethanol) of 28b showed the following absorption maxima: 218 nm (ϵ ,24,300), 290 (26,200) and 360 (24,100).

Phenylmethylglyoxal bisbenzoylhydrazone (22c) was prepared by refluxing a mixture of phenylmethylglyoxal (0.66 g, 4.05 mmol), benzhydrazide (1.4 g, 10.3 mmol) and acetic acid (1 ml) in ethanol (10 ml) for 5 hr on a water-bath. The solid which separated out on cooling was filtered off and recrystallized from a mixture (1:1) of ethanol and acetic acid to give 1.6 g (87%) of 22c, mp 252-253°.

Anal. Calcd for $C_{23}H_{20}N_4O_2$: C, 71.88; H, 5.21; N, 14.58.

Found: C, 71.80; H, 5.26; H, 14.51.

The ir spectrum (KBr) of 22c showed an amide C=O band at 1650 cm^{-1}.

The uv spectrum (ethanol) of 22c was characterized by the following absorption maxima: 224 nm (ϵ ,26,100), 294 (27,000) and 356 (24,400).

Oxidation of Benzaldehyde Benzoylhydrazone (1a)

A mixture of benzaldehyde benzoylhydrazone (1.5 g, 6.7 mmol) and nickel peroxide (2.5 g) was refluxed in chloroform (175 ml) for 4 hr. Removal of the inorganic material and the solvent gave a solid which was treated with benzene. The benzene-soluble portion was worked up separately. Recrystallization of the benzene insoluble portion from chloroform gave 0.8 g (47%) of nickel-bisbenzaldehyde benzoylhydrazone, (7a), mp 306-307°.

Anal. Calcd for $C_{28}H_{22}N_4O_2Ni$: C, 66.58; H, 4.36; N, 11.10. Found: C, 66.33; H, 4.41; N, 11.24.

The ir spectrum (KBr) of 7a showed an absorption band at 1572 cm^{-1} due to a C=N group but did not show either N-H or C=O bands.

The uv spectrum (chloroform) of 7a showed the following absorption maxima: 250 nm (ϵ ,40,000), 315 (35,700), 325 (24,000 341 (20,400), 360 (27,800), 394 (15,400) and 402 (15,000).

Magnetic moment measurements of 7a showed that the compound is diamagnetic.

The benzene-soluble portion, after removal of 7a was

chromatographed over alumina. Elution with benzene gave a product which on recrystallization from petroleum ether gave 0.45 g (30%) of 2,5-diphenyl-1,3,4-oxadiazole, (6a), mp 139-140° (lit.[2] mp 139-140°), characterized by its ir spectrum.

Oxidation of p-Tolualdehyde Benzoylhydrazone (1b)

A mixture of p-tolualdehyde benzoylhydrazone (2 g, 8.4 mmol) and nickel peroxide (4 g) was refluxed in chloroform (175 ml) for 4 hr. Removal of the inorganic material and the solvent gave a solid which was treated with benzene. The benzene-soluble portion was worked up separately. The benzene insoluble material was recrystallized from chloroform to give 0.6 g (27%) of nickel-bis-p-tolualdehyde benzoylhydrazone (7b) as orange silky needles, melting at 272-273°.

Anal. Calcd for $C_{30}H_{26}N_4O_2Ni$: C, 67.57; H, 4.88; N, 10.52. Found: C, 67.34; H, 4.99; N, 10.26.

The ir spectrum (KBr) of 7b showed an absorption band at 1580 cm^{-1} (C=N) but did not show either NH or C=O bands.

The uv spectrum of 7b in chloroform showed the following absorption maxima: 251 nm (ε ,37,600), 315 (37,600), 327 (23,800), 342 (21,200), 358 (21,100), 395 (17,000) and 408 (16,100).

The magnetic moment measurements of 7b showed it to be diamagnetic

The benzene-soluble portion after the removal of the nickel complex 7b was chromatographed over alumina. Elution with benzene gave a solid which on recrystallization from

petroleum ether gave 0.7 g (35%) of 2-phenyl-5-p-tolyl-1,3,4-oxadiazole (6b), mp 115° (lit.[17] mp 115°) as colourless needles.

Oxidation of o-Methoxybenzaldehyde Benzoylhydrazone (1c)

A mixture of o-methoxybenzaldehyde benzoylhydrazone (2 g, 7.87 mmol) and nickel peroxide (4 g) was refluxed in chloroform (200 ml) for 3 hr. Work-up of the mixture as in the earlier cases by treatment with benzene gave a benzene-insoluble product, which on recrystallization from chloroform gave 0.5 g (23%) of nickel-bis-o-methoxybenzaldehyde benzoylhydrazone (7c), mp 262-263°.

Anal. Calcd for $C_{30}H_{26}N_4O_2Ni$: C, 63.75; H, 4.60; N, 9.92. Found: C, 63.96; H, 4.72; N, 9.52.

The ir spectrum (KBr) of 7c showed an absorption band at 1582 cm^{-1} due to a C=N group but did not show any N-H or C=O bands.

The uv spectrum of 7c in chloroform showed the following absorption maxima: 250 nm (ϵ ,32,700), 310 (23,900), 317 (24,100), 324 (20,600), 340 (22,100), 355 (22,700), 369 (23,600), 404 (20,600) and 411 (20,300).

Magnetic moment measurements of 7c showed it to be diamagnetic.

The benzene-soluble portion was chromatographed over alumina. Elution with benzene gave 0.21 g (20%) of o-methoxybenzaldehyde (8), characterized through its 2,4-dinitrophenylhydrazone (0.49 g), mp 253° (mixture mp). Further elution of the column with a mixture (9:1) of benzene and ethyl acetate

gave a solid which on recrystallization from aqueous ethanol gave 0.4 g (20%) of 2-phenyl-5-(o-methoxyphenyl)-1,3,4-oxadiazole (6c), mp 96-97° (lit.[18] mp 96-97°), characterized through its infrared spectrum.

Oxidation of Anisaldehyde Benzoylhydrazone (1d)

A mixture of anisaldehyde benzoylhydrazone (1.5 g, 5.9 mmol) and nickel peroxide (3 g) was stirred in chloroform for 2½ hr at room temperature. Removal of the inorganic material and the solvent gave a solid product which was extracted with cold benzene. The benzene-insoluble portion was recrystallized from chloroform to give 0.75 g (41%) of nickel-bis-anisaldehyde benzoylhydrazone (7d), mp 289-290°.

Anal. Calcd for $C_{30}H_{26}N_4O_4Ni$: C, 63.75; H, 4.60, N, 9.92. Found: C, 63.67; H, 4.24; N, 9.66.

The ir spectrum (KBr) of 7d showed an absorption band at 1582 cm^{-1} due to a C=N group, but did not show any N-H or C=O bands.

The uv spectrum of 7d in chloroform was characterized by the following absorption maxima: 248 nm (ϵ ,35,100), 314 (34,600), 320 (37,300), 325 (26,700), 343 (24,700), 353 (27,100), 398 (27,900) and 412 (27,100).

Magnetic moment measurement of 7d showed it to be diamagnetic.

The benzene-soluble portion after the removal of 7d was worked-up as in the earlier cases to give a solid which on recrystallization from a mixture (1:1) of petroleum ether and

benzene gave 0.4 g (21%) of 2-phenyl-5-anisyl-1,3,4-oxadizole (6d), mp 151-152° (lit.[18] mp 151-152°), characterized through its infrared spectrum.

Oxidation of Acetophenone Benzoylhydrazone (10a)

A mixture of acetophenone benzoylhydrazone (2 g, 8.4 mmol) and nickel peroxide (4 g) was refluxed in benzene (175 ml) for 4 hr. Work-up of the mixture in the usual manner gave a viscous liquid which was chromatographed over alumina. Elution with a mixture (4:1) of petroleum ether and benzene gave 0.36 g (36%) of acetophenone (15a), isolated as its 2,4-dinitrophenylhydrazone derivative (0.9 g), mp 237° (mixture mp). Further elution of the column with the same solvent mixture gave a solid which on recrystallization from a mixture (3:1) of alcohol and benzene gave 0.2 g (11%) of a colourless solid melting at 249-250° and identified as methyl-benzylidene-α-dibenzoylamino-α-methylbenzylamine (20a).

Anal. Calcd for $C_{30}H_{26}N_2O_2$: C, 80.72; H, 5.80; N, 6.25; Mol. wt., 446. Found: C, 80.83; H, 6.16; H, 6.14; Mol. wt., 446 (mass spectrometry).

The ir spectrum (KBr) of 20a showed the following absorption bands at 1675 cm^{-1} (C=O), 1670 cm^{-1} (C=O) and 1640 (C=N) cm^{-1}.

The uv spectrum (ethanol) of 20a was characterized by the following absorption maxima: 230 nm (ε, 17,900), 280 (14,000) and 292 (12,400).

The nmr spectrum ($CDCl_3$) of 20a showed signals at 1.73 δ(3H, singlet, methyl protons), 1.87 δ(3H, singlet, methyl protons) and 7.0-8.2 δ(20H, multiplet, aromatic protons).

Hydrolysis of Methylbenzylidene-α-dibenzoylamino-α-methylbenzylamine (20a)

A mixture of 20a (0.1 g, 0.022 mmol) and sodium hydroxide (0.1 g, 2.5 mmol) was refluxed in ethylene glycol (10 ml) for 8 hr and later poured into ice-cold water. The solid (60 mg) which separated out was filtered and then recrystallized from ethanol to give 50 mg (66%) of methylbenzylidene-α-benzoylamino-α-methylbenzylamine (21), mp 164-165°.

Anal. Calcd for $C_{23}H_{22}N_2O$: C, 80.70; H, 6.43; N, 8.18; Mol. wt., 342. Found: C, 80.94; H, 6.27; N, 8.32; Mol. wt., 342 (mass spectrometry).

The ir spectrum (KBr) of 21 showed the following absorption bands at 3308 cm^{-1} (N-H), 1640 (C=O), amide) and 1633 (C=N).

The uv spectrum of 21 ethanol showed an absorption maximum at 286 nm (ε, 11,700).

The nmr spectrum ($CDCl_3$) of 21 showed chemical shifts at 1.33 δ(3H, singlet, methyl protons), 1.66 δ(3H, singlet, methyl protons), 5.23 δ(1H, broad singlet, N-H proton) and 7.65 δ(15H, multiplet, aromatic protons).

Oxidation of Propiophenone Benzoylhydrazone (10b)

A mixture of propiophenone benzoylhydrazone (2 g, 7.94 mmol) and nickel peroxide (3.5 g) was refluxed in benzene

(175 ml) for 4 hr. Removal of the inorganic material and the solvent in the usual manner gave a viscous liquid which was chromatographed over alumina. Elution with a mixture (4:1) of petroleum ether and benzene gave 0.45 g (40%) of propiophenone (15b) isolated through its 2,4-dinitrophenylhydrazine derivative (1 g), mp 187-189° (mixture mp). Further elution of the column with a mixture (1:1) of petroleum ether and benzene gave a solid which on recrystallization from a mixture (3:1) of ethanol and benzene gave 0.15 g (8%) of ethylbenzylidene-α-dibenzoyl-amino-α-ethylbenzylamine (20b), mp 262-263°.

Anal. Calcd for $C_{32}H_{30}N_2O_2$: C, 81.00; H, 6.33; N, 5.91; Mol. wt.,474. Found: C, 80.68; H, 6.52; N, 5.85; Mol. wt.,474 (mass spectrometry).

The ir spectrum (KBr) of 20b showed the following absorption bands at 1660 cm^{-1} (C=O) and 1635 cm^{-1} (C=N).

The uv spectrum of 20b in cyclohexane was characterized by the following absorption maxima: 223 nm (ε,33,300), 286 (14,400) and 295 (14,200).

The nmr spectrum ($CDCl_3$) of 20b showed signals at 0.54 δ(3H, triplet, methyl protons), 0.99 δ(3H, triplet, methyl protons), 2.17 δ(2H, quartet, methyl protons), 2.23 δ(2H, quartet methylene protons) and 7.49 δ(20H, multiplet, aromatic protons).

Oxidation of Benzophenone Benzoylhydrazone (10c)

Refluxing a mixture of benzophenone benzoylhydrazone (1.5 g, 5.0 mmol) and nickel peroxide (3 g) in benzene (175 ml) for 4 hr and work-up in the usual manner gave a viscous liquid

which was chromatographed over alumina. Elution with a mixture (4:1) of petroleum ether and benzene gave 0.45 g (50%) of benzophenone (15c) isolated as its 2,4-dinitrophenylhydrazone derivative, mp 238° (mixture mp). Further elution of the column with a mixture (1:1) of petroleum ether and benzene gave 0.15 g (16%) of phenylbenzylidene-α-dibenzoylamino-α-phenylbenzylamine (20c), mp 168-169°.

Anal. Calcd for $C_{40}H_{30}N_2O_2$: C, 84.21; H, 5.26; N, 4.91; Mol. wt., 570. Found: C, 84.26; H, 5.38; N, 5.03; Mol. wt., 570 (mass spectrometry).

The ir spectrum (KBr) of 20c showed the following absorption bands at 1655 cm^{-1} (C=O) and 1600 cm^{-1} (C=N), respectively.

The uv spectrum (cyclohexane) of 20c showed the following absorption maxima: 230 nm (ϵ 33,100) and 313 (7,000).

The nmr spectrum ($CDCl_3$) of 20c showed a multiplet centred at 7.39 δ(30H) due to the aromatic protons.

Oxidation of Biacetyl Bisbenzoylhydrazone (22a)

A mixture of biacetyl bisbenzoylhydrazone (1.5 g, 4.7 mmol) and nickel peroxide (5 g) was refluxed in chloroform for 4 hr. Removal of the inorganic material and the solvent as in the previous cases gave a solid which was extracted with a mixture of benzene and chloroform. The residual solid was recrystallized from chloroform to give 0.4 g (24%) of nickel-biacetyl bisbenzoylhydrazone (27a), mp 284-285° (mixture mp).[19]

The filtrate after removal of the nickel complex 27a

was chromatographed over alumina. Elution with benzene gave 0.1 g (7%) of 1-α-benzoyloxybenzylideneamino-4,5-dimethyl-1,2,3-triazole (26a), mp 139-140° (mixture mp).[7]

Oxidation of Benzil Bisbenzoylhydrazone (22b)

A mixture of benzil bisbenzoylhydrazone (2 g, 4.5 mmol) and nickel peroxide (4 g) was refluxed in chloroform (175 ml) for 4 hr. Work-up of the mixture as in the earlier cases gave a product which was extracted with a mixture of benzene and chloroform. The residual solid was recrystallized from chloroform to give 0.5 g (22%) of nickel-benzil bisbenzoylhydrazone (27b), mp 300-301°.

Anal. Calcd for $C_{28}H_{20}N_4O_2Ni$; C, 66.83; H, 3.98; H, 11.14; Ni, 11.68. Found: C, 66.53; H, 3.58; H, 11.50; Ni, 11.83.

The ir spectrum (KBr) of 27b showed an absorption bands at 1600 cm^{-1} due to C=N but did not show the presence of either N-H or C=O bands.

The uv spectrum of 27b in chloroform showed the following absorption maxima: 292 nm (ε,20,800), 340 (16,800), 358 (17,800), 392 (19,900), 404 (19,200) and 424 (15,100).

Magnetic moment measurements of 27b showed it to be diamagnetic.

The benzene-chloroform soluble portion after the removal of 24b was chromatographed over alumina. Elution with benzene gave 0.5 g (26%) of 1-α-benzoyloxybenzylideneamino-4,5-diphenyl-1,2,3-triazole (26b), mp 188-189° (mixture mp).[7]

Further elution of the column with the same solvent gave 0.6 g (30%) of the unchanged starting material (22b), mp 206° (mixture mp).

Oxidation of Phenylmethylglyoxal Bisbenzoylhydrazone (22c)

Refluxing a mixture of phenylmethylglyoxal bisbenzoylhydrazone (1 g, 2.6 mmol) and nickel peroxide (3 g) in chloroform (150 ml) for 4 hr and work-up in the usual manner gave a product mixture which on subsequent treatment with ethanol gave a colourless solid. Recrystallization of this solid from a mixture (2:1) of petroleum ether and benzene gave 0.25 g (25%) of 1-α-benzoyloxybenzylideneamino-4-phenyl-5-methyl-1,2,3-triazole (26c), mp 165-166°.

Anal. Calcd for $C_{23}H_{18}N_4O_2$: C, 72.24; H, 4.71; N, 14.66. Found: C, 72.30; H, 4.50; H, 14.35.

The ir spectrum (KBr) of 26c showed the following absorption bands at 1750 cm^{-1} (C=O, ester) and 1640 cm^{-1} (C=N).

The uv spectrum of 26c in ethanol showed the following characteristic absorption maxima: 245 nm (ε 30,500), 256 (27,300) and 329 (3,000).

Oxidation of Phenylglyoxal Bisbenzoylhydrazone (28a)

A mixture of phenylglyoxal bisbenzoylhydrazone (1.5 g, 4.1 mmol) and nickel peroxide (4 g) was refluxed in chloroform (200 ml) for 3 hr. Work-up in the usual manner gave a solid which was extracted with cold benzene. The benzene-insoluble portion was recrystallized from benzene to give 0.3 g (19%) of nickel-bis-phenyl-2-(5-phenyl-1,3,4-oxadiazolyl)-ketone benzoyl-

hydrazone (38a), mp 321-322°.

Anal. Calcd for $C_{44}H_{30}N_8O_4Ni$: C, 66.62; H, 3.78; N, 14.13. Found: C, 66.38; H, 3.76; N, 13.73.

The ir spectrum (KBr) of 38a showed an absorption band at 1595 cm^{-1} due to C=N but did not show the presence of either N-H or C=O bands.

The uv spectrum of 38a in chloroform was characterized by the following absorption maxima: 288 nm (ϵ,33,600) and 426 (87,900).

Magnetic moment measurement of 38a showed it to be diamagnetic.

The benzene-soluble portion, after the removal of the nickel complex 38a was chromatographed over alumina. Elution with a mixture (1:4) of petroleum ether and benzene gave an additional amount (0.2 g, 12%) of 38a, mp 321-322° (mixture mp). Further elution of the column with benzene gave a solid which was recrystallized from a mixture (5:1) of benzene and alcohol to give 0.35 g (23%) of 1-dibenzoylamino-4-phenyl-1,2,3-triazole (33a), mp 213-214°.

Anal. Calcd for $C_{22}H_{16}N_4O_2$: C, 71.74; H, 4.35; N, 15.22. Found: C, 71.78; H, 3.96; N, 15.37.

The ir spectrum (KBr) of 30a showed an absorption band at 1692 cm^{-1} due to an amide C=O group.

The uv spectrum of 33a in ethanol showed the following absorption maxima: 230 nm (ϵ,16,900), 284 (16,300) and 336 (21,400).

Further elution of the column with ethanol gave a solid which on recrystallization from aqueous methanol gave 0.1 g (7%) of 1-benzoylamino-4-phenyl-1,2,3-triazole (34a), mp 217-218° (mixture mp).[14]

Oxidation of 4-Methoxyphenylglyoxal Bisbenzoylhydrazone (28b)

A mixture of 4-methoxyphenylglyoxal bisbenzoylhydrazone (1.5 g, 3.7 mmol) and nickel peroxide (5 g) was refluxed in chloroform (200 ml) for 3 hr. Removal of the inorganic material and the solvent gave a semi-solid which was chromatographed over alumina. Elution with benzene gave a solid which was recrystallized from benzene to give 0.1 g (6%) of a brown amorphous powder which was characterized as nickel-bis-4-methoxyphenyl-2-(5-phenyl-1,3,4-oxadiazolyl)-ketone benzoylhydrazone (38b), mp 361-362°(d).

Anal. Calcd for $C_{46}H_{34}N_8O_6Ni$: C, 64.74; H, 4.00; N, 13.13. Found: C, 64.43; H, 4.03; H, 12.77.

The ir spectrum (KBr) of 38b showed an absorption bands at 1600 cm^{-1} due to a C=N group but did not show either N-H or C=O band absorptions.

The uv spectrum of 38b in chloroform showed the following absorption maxima at 306 nm (ϵ ,37,600) and 432 (54,200), respectively.

Magnetic moment measurement of 38b showed it to be diamagnetic.

Further elution of the column with benzene gave a solid which on recrystallization from a mixture (2:1) of petroleum

ether and benzene gave 0.1 g (7%) of 1-dibenzoylamino-4-(4-methoxyphenyl)-1,2,3-triazole (33b), mp 225-226°.

Anal. Calcd for $C_{23}H_{18}N_4O_3$: C, 69.34; H, 4.52; N, 14.07. Found: C, 69.67; H, 4.63; N, 14.23.

The ir spectrum (KBr) of 33b showed the presence of an amide carbonyl at 1695 cm^{-1}.

The uv spectrum of 33b in ethanol showed the following absorption maxima: 239 nm (ε,20,850), 295 (19,800) and 348 (17,600).

Subsequent elution of the column with ethanol gave a solid which on recrystallization from aqueous ethanol gave 0.1 g (9%) of 1-benzoylamino-4-(4-methoxyphenyl)-1,2,3-triazole (34b), mp 200-201°.

Anal. Calcd for $C_{16}H_{14}N_4O_2$: C, 65.31; H, 4.76; N, 19.05. Found: C, 65.07; H, 5.06; N, 18.71.

The ir spectrum (KBr) of 34b showed absorption bands at 3250 cm^{-1} (N-H) and 1690 cm^{-1} (amide (C=O).

The uv spectrum of 34b in ethanol showed an absorption maximum at 256 nm (ε ,27,300).

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CHAPTER V

OXIDATION OF SCHIFF'S BASES, HYDRAZINES AND AMINES WITH NICKEL PEROXIDE

V.1 ABSTRACT

N-Benzylidene-o-phenylenediamine, on oxidation with nickel peroxide, gives 2-phenylbenzimidazole. Similarly, benzimidazole derivatives have been obtained from 2-nitro-, 3-nitro- and 4-nitrobenzylidene-o-phenylenediamines. The oxidation of 2-hydrazinobenzothiazole with nickel peroxide gives different products depending on the nature of the solvent employed in these reactions. Thus, the oxidation of 2-hydrazinobenzothiazole with nickel peroxide, in benzene, gives a mixture of biphenyl, benzothiazole and 2-phenylbenzothiazole. In toluene, however, the products formed are benzothiazole, 2,2'-bisbenzothiazolyl and a small amount of benzaldehyde. When the oxidation of 2-hydrazinobenzothiazole is carried out in chloroform, only benzothiazole and 2,2'-azodibenzothiazolyl could be isolated. The oxidation of N-aminophthalimide with

nickel peroxide gives phthalimide as the only isolable product. N-(2-Aminophenyl)-pyrrolidine, on oxidation with nickel peroxide, gives a mixture of 1,2-trimethylenebenzimidazole and 2,2'-di-(N-pyrrolidino)-azobenzene.

V.2 RESULTS AND DISCUSSION

In continuation of our studies using nickel peroxide as an oxidizing agent for the oxidation of different organic substrates, we have examined the oxidation of o-aminobenzylideneanils, substituted hydrazines and other related compounds, employing this reagent.

It has been reported that o-hydroxybenzylideneanils are oxidized by nickel peroxide,[1] manganese dioxide[2] and lead tetraacetate[3] to give the corresponding benzoxazole derivatives. Similarly, N-benzylidene-o-phenylenediamines have been oxidized by a variety of reagents like manganese dioxide,[2] lead tetraacetate,[3] air[4] and mercuric oxide.[5] The products from the oxidations have been characterized as benzimidazole derivatives. N-Benzylidene-o-phenylenediamine, for example, is oxidized to 2-phenylbenzimidazole by mere refluxing in ethanol or ether in presence of air.[4] The same product has been obtained when N-benzylidene-o-phenylenediamine is heated in dilute hydrochloric acid in presence of air.[4b] On the other hand, N-benzylidene-o-phenylenediamine disproportionates into a mixture of 2-phenylbenzimidazole and N-benzyl-o-phenylenediamine when heated to

around 180-230° in the absence of air.[6] Similarly, lead tetraacetate[3] and mercuric oxide[5] oxidations of N-benzylidene-o-phenylenediamines are reported to give the corresponding benzimidazoles.

During the course of the present investigation, we have examined the oxidation of a few N-benzylidene-o-phenylenediamines with nickel peroxide. Thus, the oxidation of N-benzylidene-o-phenylenediamine (1a) with nickel peroxide, in benzene, at room temperature, gives a 71% yield of 2-phenylbenzimidazole (4a). Similarly, the oxidation of o-nitro-, m-nitro- and p-nitrobenzylidene-o-phenylenediamines (1b-d) gives the corresponding benzimidazoles 4b-d, in yields ranging between 41-57% (Scheme V.1).

The formation of benzimidazoles 4a-d in the oxidation of N-benzylidene-o-phenylenediamines 1a-d can be explained in terms of the reaction sequences shown in Scheme V.1. In this scheme, we assume that nickel peroxide abstracts a proton from 1 giving rise to the radical intermediate 2 which then undergoes cyclization to give the radical intermediate 3. Further oxidation of 3 would result in the formation of benzimidazoles 4.

In continuation of our studies, we have examined the oxidation of 2-hydrazinobenzothiazole with nickel peroxide, in different solvents. It has been reported that phenylhydrazine has been oxidized by reagents such as silver oxide,[7] mercuric oxide,[7] lead tetraacetate[8] and manganese dioxide[9] to give

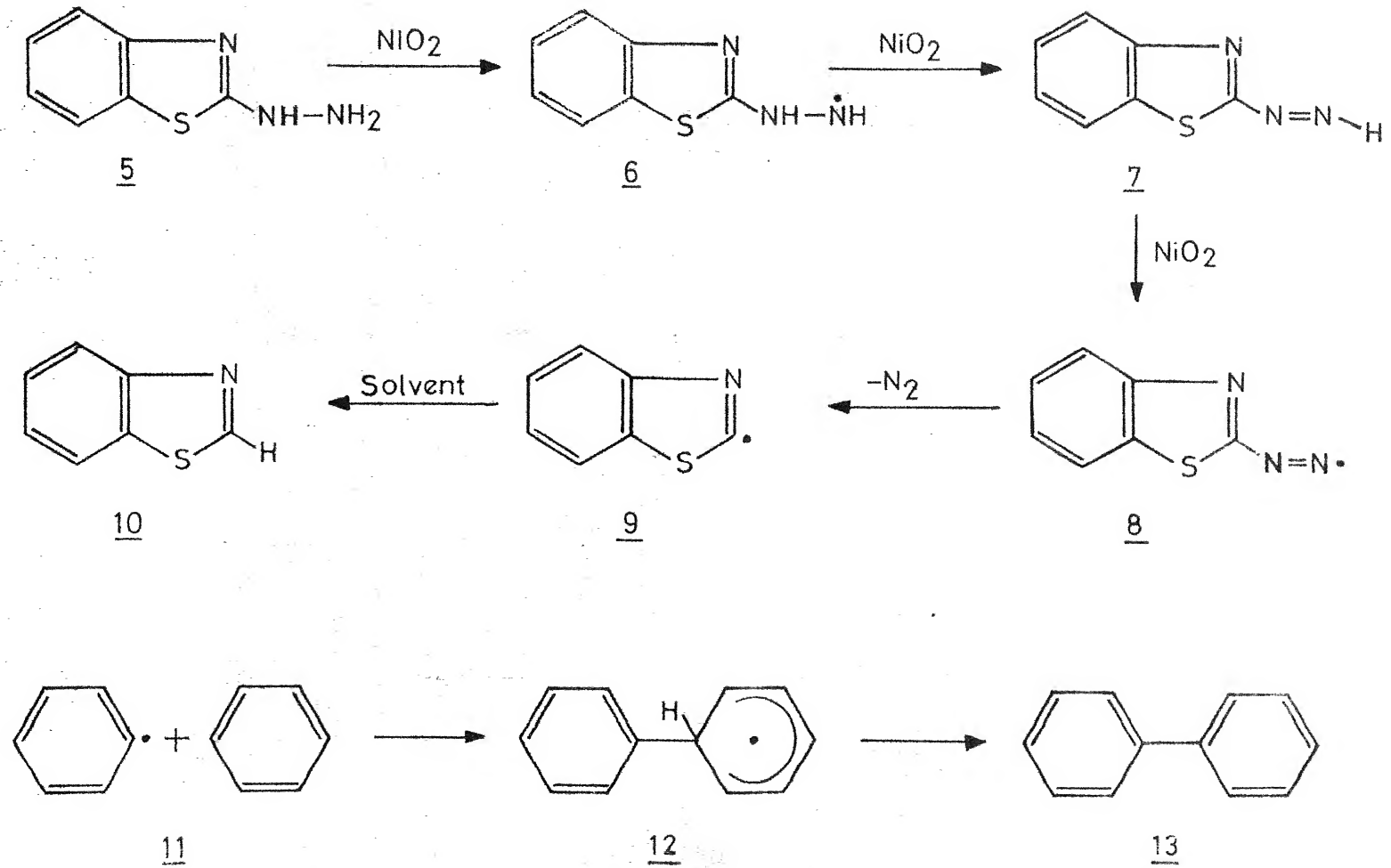
biphenyl as the chief product. Recently, nickel peroxide has been used for the oxidation of phenylhydrazine and it has been shown that the products obtained in this reaction depend largely on the nature of the solvent employed.[10] Thus, in cyclohexane medium, both benzene and biphenyl are formed.[10] In carbon tetrachloride, however, the products formed are chlorobenzene, small amounts of benzene, biphenyl and hexachloroethane.[10] On the other hand, when the reaction is carried out in benzene, the products formed are biphenyl, small amounts of 1,4-dihydrobiphenyl and phenol.[10] In a solvent such as toluene, an isomeric mixture of o-, m- and p-methylbiphenyls is formed. The formation of these various products in the oxidation of phenylhydrazine has been explained in terms of phenyl radicals, formed in these reactions which can undergo a variety of reactions like hydrogen abstraction, addition to benzene, dimerization, etc.

In the present studies, we have examined the oxidation of 2-hydrazinobenzothiazole (5), with nickel peroxide in different solvents, to study the nature of the products formed in these cases. Treatment of a mixture of 2-hydrazinobenzothiazole (5) with nickel peroxide, in benzene, gives a 28% yield of 2-phenylbenzothiazole (15) and a 12% yield of benzothiazole (10) together with traces of biphenyl. When the oxidation of 5 is carried out in toluene, the products that could be isolated

are a 55% yield of benzothiazole (10), a 3% yield of 2,2'-dibenzothiazolyl (16) and a 18% yield of benzaldehyde. In contrast, the oxidation of 5 with nickel peroxide, in chloroform solution, gives a 14% yield of benzothiazole (10) and a 11% yield of 2,2'-azodibenzothiazole (17) (Scheme V.2).

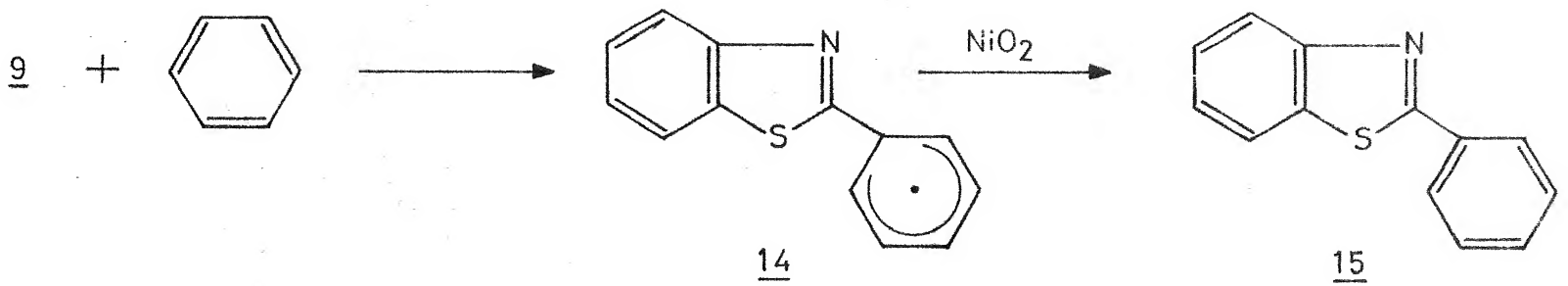
The formation of products such as 10, 13, 15, 16 and 17 in the oxidation of 2-hydrazinobenzothiazole (5), with nickel peroxide, in different solvents like benzene, toluene and chloroform can be rationalized in terms of the reaction sequences shown in Scheme V.2. In this scheme, we assume that nickel peroxide abstracts a proton from 5 giving rise to the radical intermediate 6 which is then converted to the benzothiazolyldiimide 7. Further oxidation of 7 will lead to the intermediate 8 which can lose nitrogen to give the benzothiazolyl radical 9. This radical, in turn, will pick up a proton from either the solvent or the starting hydrazine to give benzothiazole 10. The formation of biphenyl (13) in these reactions may be explained in terms of the reaction of phenyl radical intermediates with benzene, which is used as the solvent. Phenyl radicals themselves may be formed by the interaction of one of the intervening radicals shown in Scheme V.2 with the solvent, followed by fragmentation of the products formed in these reactions. Similarly, the formation of 2-phenyl-

Scheme V·2

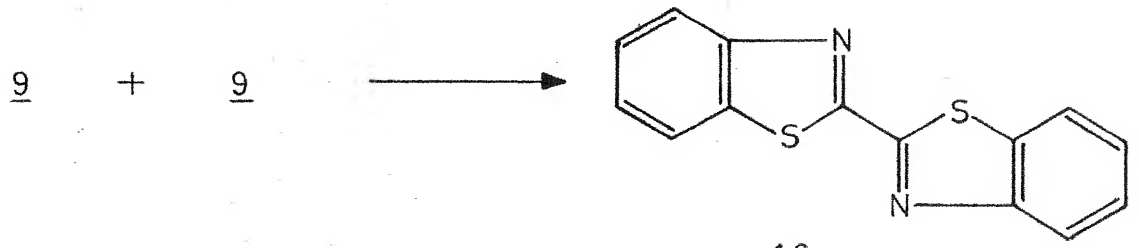


5 6 7 8 9 10 11 12 13

Scheme V·2 (Contd.)



14 15



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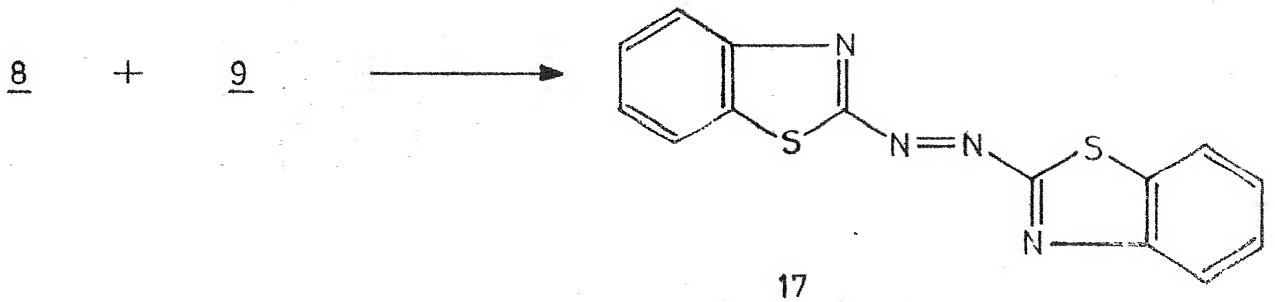


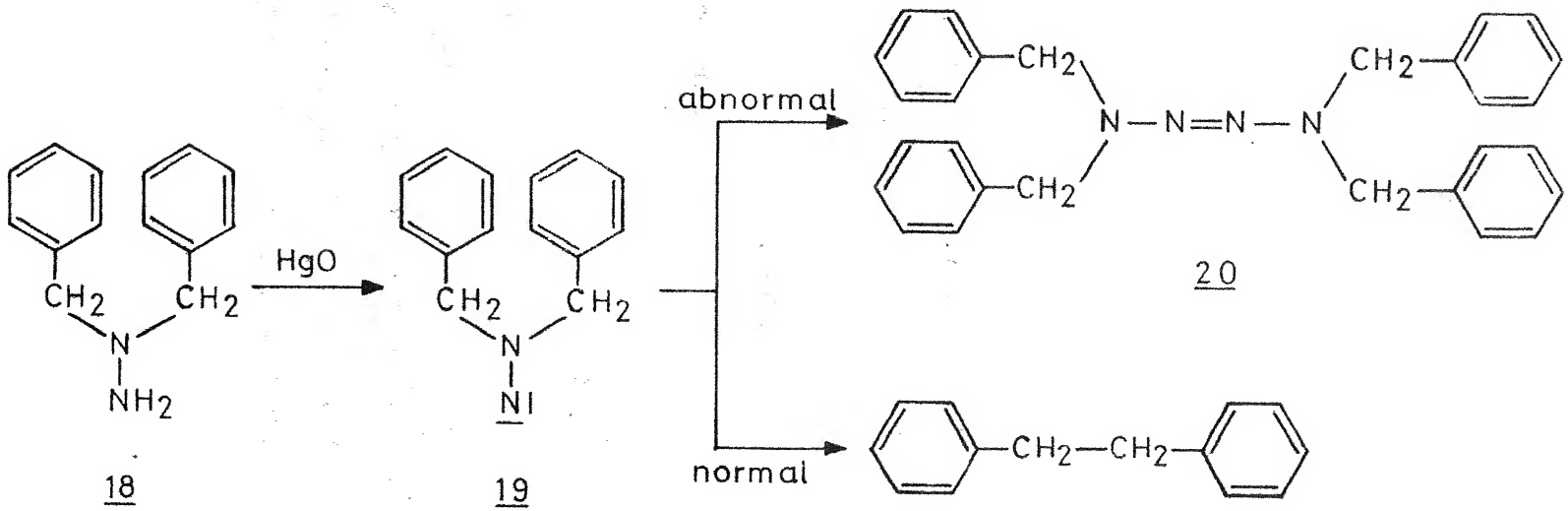
17

benzothiazole (15) may be through the interaction of the radical intermediate 9 with benzene to give 14, which can subsequently lose a hydrogen atom as shown in Scheme V.2. Coupling of two benzothiazolyl radicals (9) will lead to 2,2'-dibenzothiazolyl (16), whereas, the coupling of radical intermediates 8 and 9 would lead to the formation of 2,2'-azodibenzothiazole (17). The formation of benzaldehyde in the oxidation employing toluene may occur through the oxidation of the solvent itself. Such oxidations of hydrocarbons containing benzylic side chains by nickel peroxide are known to occur readily.[11]

Several 1,1-disubstituted hydrazines have been oxidized with different oxidizing agents, such as potassium permanganate, bromine, tert-butylhypochlorite, mercuric oxide, lead tetraacetate, manganese dioxide and nickel peroxide to give the corresponding tetrazenes as major products.[12-14] Report has also been made of an anomalous type of oxidation of 1,1-disubstituted hydrazines giving rise to symmetrically substituted bibenzyls and nitrogen or coupling products.[11] A detailed study of the oxidation of 1,1-disubstituted hydrazine derivatives has been carried out by several groups of workers.[1] In general, it has been observed that when the oxidation of a 1,1-disubstituted hydrazine is carried out under conditions in which the hydrazine is present in relatively high concen-

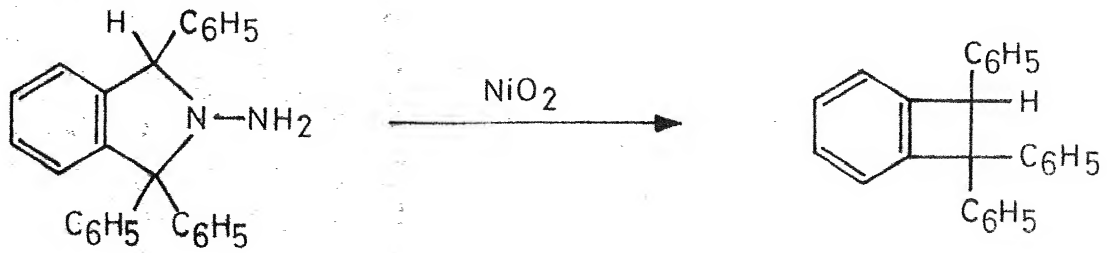
tration, as in the case of rapid addition of hydrazine to the oxidizing agent or by the rapid addition of the solid oxidizing agent to the solution of hydrazine, the azamine intermediate formed initially dimerizes to the tetrazene in the so-called "normal" manner. If the nitrogen atom in the azamine intermediate is lost to yield a stabilized radical, then an alternative "abnormal" pathway is possible, which would lead to fragmentation and recombination of products. The oxidation of 1,1-dibenzylhydrazine (18), for example, gives rise to mainly,bibenzyl (21) and nitrogen and an intramolecular process has been suggested for this reaction (Scheme V.3). The formation of the tetrazene 20 is explained in terms of the dimerization of the azamine intermediate 19 or by its reaction with another molecule of hydrazine to give a tetrazane derivative which is subsequently oxidized to the tetrazene.[12a,b] The formation of the azamine intermediate in the oxidation of 1,1-disubstituted hydrazines has been clearly shown by trapping the intermediates with olefins leading to aziridine derivatives.[12a] In the oxidation of a compound such as N-amino-1,1,3-triphenylisoindoline (22) with nickel peroxide, it has been reported that oxidative fragmentation occurs which leads to the formation of 1,1,2-triphenylbenzocyclobutene (23) (Scheme V.4).[15] In the present studies, we have oxidized N-aminophthalimide (24) with nickel peroxide, in refluxing benzene. The chief

Scheme V·3



18 19 20 21

Scheme V·4



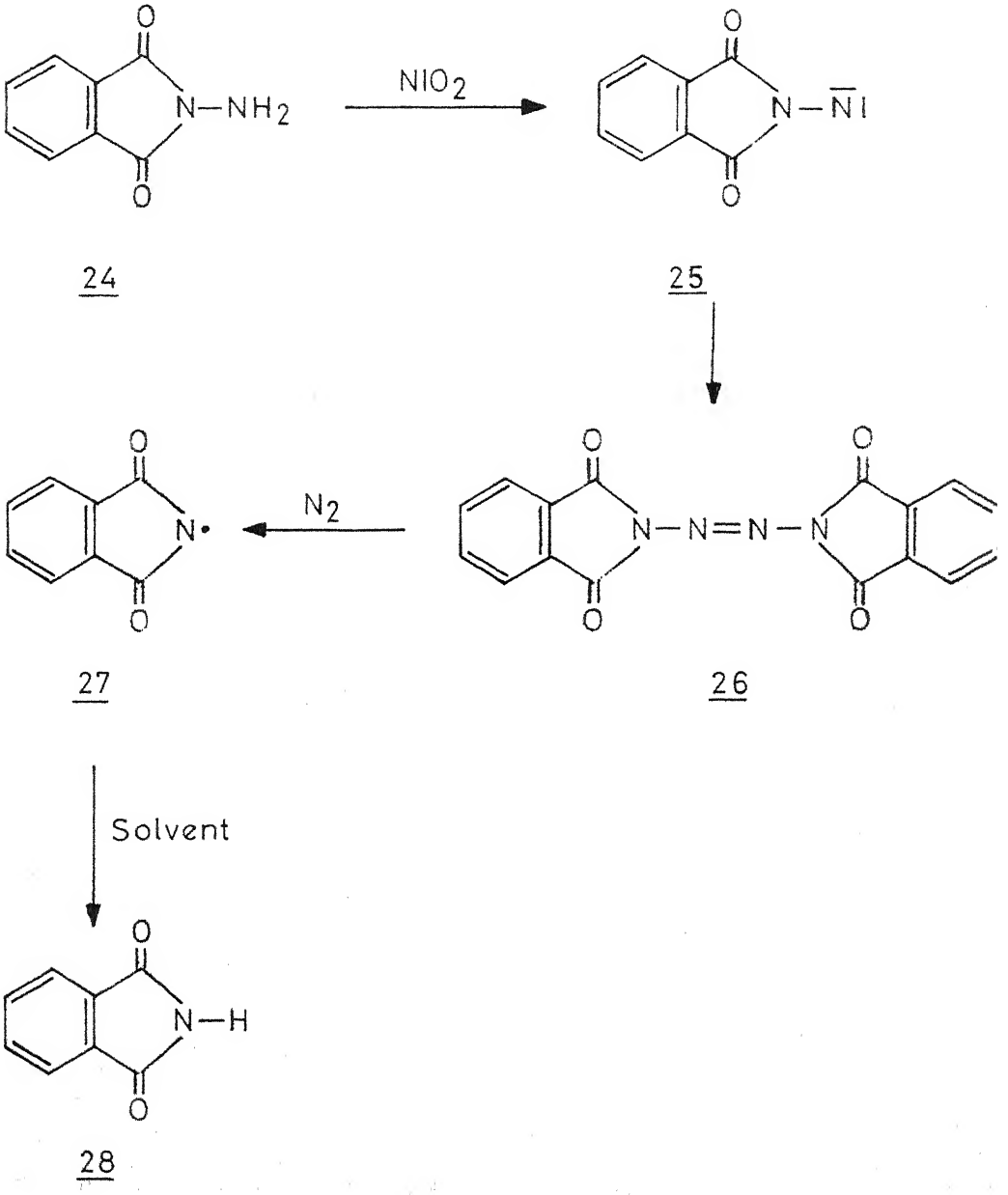
22 23

product that could be isolated from this reaction has been phthalimide (28). In addition, a small amount of biphenyl and some unchanged starting material could also be recovered. However, none of the expected tetrazene or other coupling products could be isolated from this run.

The formation of phthalimide (28) in the oxidation of N-aminophthalimide (24) can be explained as per Scheme V.5. In this scheme, we assume that nickel peroxide abstracts two hydrogen atoms from 24 giving rise to the azamine intermediate 25. Dimerization of 25 or its reaction with another molecule of N-aminophthalimide (24), followed by oxidation, gives the tetrazene derivative 26. Loss of a molecule of nitrogen from 26 results in the radical intermediate 27 which then picks up a hydrogen atom from either the solvent or the starting hydrazine to give phthalimide (26).

The oxidation of tertiary amines with manganese dioxide has been studied in detail and three important pathways are observed in the conversion of these substances to various products shown in Scheme V.6.[16-19] The oxidation of N,N-dimethylaniline, for example, gives chiefly N-methylformanilide and this reaction may be proceeding through route (a) shown in Scheme V.6. On the other hand, the oxidation of diethylaniline proves to be more complex. The predominant reaction is by route (b) to give both N-ethylaniline and acetaldehyde.

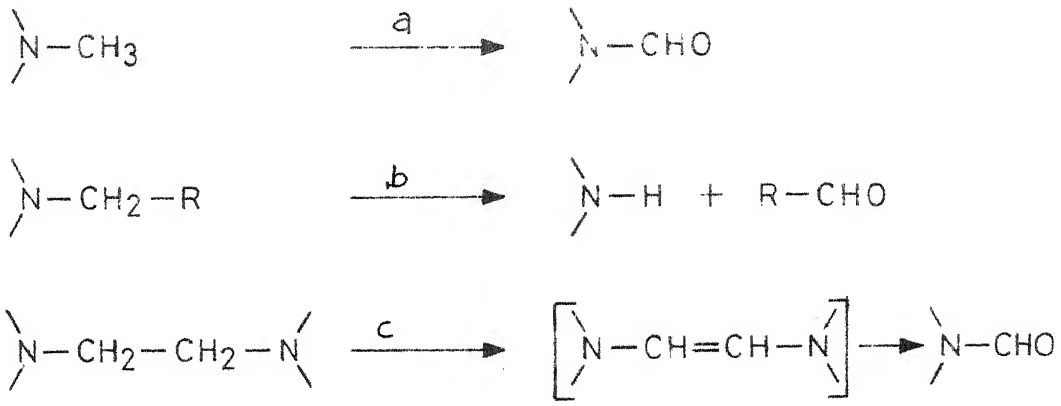
Scheme V 5



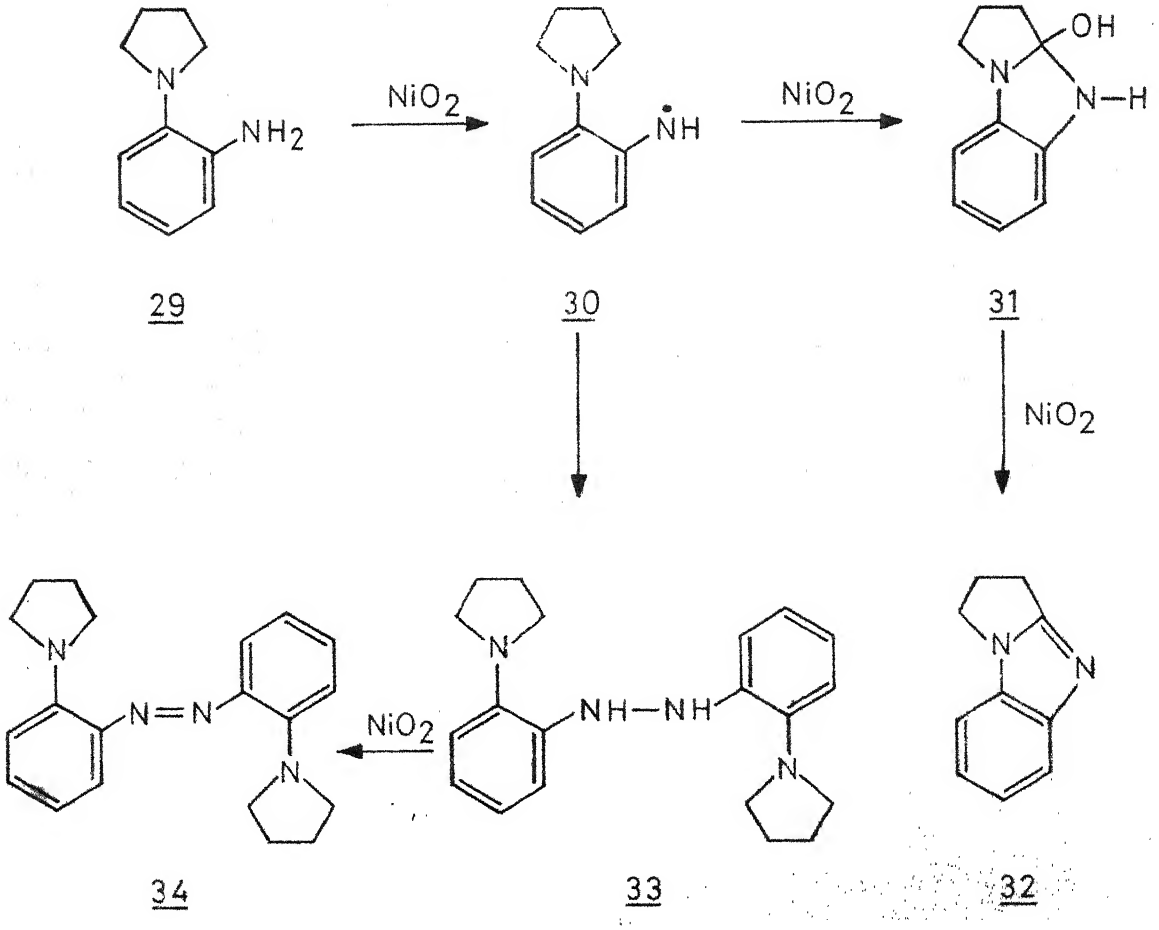
24 25 26 27 28

The N-ethylaniline, thus formed, may undergo further oxidation by route (c) to give formanilide. Small amounts of N-ethylformanilide, azobenzene and acetaldehyde are also formed in this reaction. As would be expected, N-ethyl-N-methylaniline gives both N-ethylformanilide and formanilide, probably, through routes (a) and (b). Meth-Cohn and coworkers have used this reaction for the oxidative cyclization of N,N-dialkyl-o-phenylenediamines with manganese dioxide to give benzimidazole derivatives.[20] This type of oxidative cyclization has been reported using Caro's acid,[21] peroxytrifluoroacetic acid,[22] formic acid and hydrogen peroxide.[23] In the course of the present investigation, we have examined the oxidation of N-(2-aminophenyl)-pyrrolidine (29), with nickel peroxide, to study the nature of the products formed in this case. Treatment of N-(2-aminophenyl)-pyrrolidine (29), with nickel peroxide, in benzene, at room temperature, gives a 3% yield of 1,2-trimethylenebenzimidazole (32) and a 10% yield of a red compound, melting at 177-178°, identified as the oxidative dimer 34 (Scheme V.7). The structure of 34 has been established on the basis of analytical data and spectral evidences. Compound 34 analyzes for $C_{20}H_{24}N_4$ and its uv spectrum shows several absorption maxima at 226 nm (ϵ,23,100), 275 (17,850), 311 (5,950), 472 (10,700), 502 (13,000) and 530 (11,500) indicating the presence of a conjugated chromophore as in azobenzene.

Scheme V·6



Scheme V·7



29 30 31 32 33 34

A probable route to the formation of both 32 and 34 in the oxidation of 29 is shown in Scheme V.7. In this scheme, we assume that nickel peroxide first oxidizes the NH_2 group to give the radical intermediate 30, which can then be oxidized to 32, through the intermediate 31. A second possible route for the reaction of 30 is through a dimerization reaction leading to the hydrazobenzene derivative 33. Further oxidation of 33, with nickel peroxide under the reaction conditions, will lead to 34 as shown in Scheme V.7. It might be pointed out here that other possible pathways for the formation of the cyclic intermediate 31 arising through the initial hydroxylation of the methylene group in the pyrrolidine side chain can also be formulated.

V.3 EXPERIMENTAL

Starting Materials

N-Benzylidene-o-phenylenediamine, mp 60-61°,[4b] N-(2-nitrobenzylidene)-o-phenylenediamine, mp 93-94°,[4a] N-(3-nitrobenzylidene)-o-phenylenediamine, mp 108°,[3a] N-(4-nitrobenzylidene)-o-phenylenediamine, mp 134°,[4a] N-aminophthalimide, mp 204°,[24] N-(2-aminophenyl)-pyrrolidine, mp 73-75°,[23] were prepared as per reported procedures. 2-Hydrazinobenzothiazole was obtained from Eastman Organic Chemicals.

Oxidation of N-Benzylidene-o-phenylenediamine (1a)

A mixture of N-benzylidene-o-phenylenediamine (2 g, 10.2 mmol) and nickel peroxide (4 g) was stirred in benzene for 3 hr at room temperature. Removal of the inorganic material by filtration and the solvent under vacuum gave a solid which was recrystallized from a mixture (1:1) of benzene and ethanol to give 1.4 g (71%) of 2-phenylbenzimidazole (4a), 287-288° (mixture mp).[24]

Oxidation of N-(2-Nitrobenzylidene)-o-phenylenediamine (1b)

A mixture of N-(2-nitrobenzylidene)-o-phenylenediamine (1.5 g, 6.22 mmol) and nickel peroxide (4 g) was stirred in benzene for 3 hr at room temperature. Removal of the inorganic material and of the solvent gave a viscous mass which was chromatographed over alumina. Elution with a mixture (1:2) of petroleum ether and benzene gave 0.6 g (41%) of 2-(o-nitrophenyl)-benzimidazole (4b), mp 263° (mixture mp).[25]

Oxidation of N-(3-Nitrobenzylidene)-o-phenylenediamine (1c)

N-(3-nitrobenzylidene)-o-phenylenediamine (1.5 g, 6.22 mmol) and nickel peroxide (4 g) were stirred in benzene (200 ml) for 4 hr at room temperature. Work-up of the mixture in the usual manner gave a viscous mass which was chromatographed over alumina. Elution with a mixture (1:3) of petroleum ether and benzene gave a solid which on recrystallization from

aqueous ethanol gave 0.72 g (49%) of 2-(m-nitrophenyl)-benzimidazole (4c), mp 204-205° (mixture mp).[3a]

Oxidation of N-(4-Nitrophenyl)-o-phenylenediamine (1d)

A mixture of N-(4-nitrophenyl)-o-phenylenediamine (1.5 g, 6.22 mmol) and nickel peroxide (4 g) was stirred in benzene for 4 hr at room temperature. Removal of the inorganic material and the solvent gave a solid which on recrystallization from ethanol gave 0.85 g (57%) of 2-(p-nitrophenyl)-benzimidazole (4d), mp 329-330° (mixture mp).[3a]

Oxidation of 2-Hydrazinobenzothiazole (5)

A In Refluxing Benzene

A mixture of 2-hydrazinobenzothiazole (2 g, 12.1 mmol) and nickel peroxide (10 g) was refluxed in benzene (200 ml) for 4 hr. Removal of the inorganic material and the solvent gave a viscous liquid which was chromatographed over alumina. Elution with petroleum ether gave 25 mg (2%) of biphenyl, mp 70° (mixture mp). Further elution of the column with a mixture (4:1) of petroleum ether and benzene gave a solid which was recrystallized from ethanol to give 0.7 g (28%) of 2-phenylbenzothiazole (15), mp 114° (lit.[26] mp 114°). Subsequent elution of the column with a mixture (1:1) of benzene and petroleum ether gave 0.2 g (12%) of a liquid, bp 223-225°, which was characterized as benzothiazole (10) by comparing with an authentic sample.

B In Refluxing Toluene

A mixture of 2-hydrazinobenzothiazole (2 g, 12.1 mmol) and nickel peroxide (10 g) was refluxed in dry toluene (200 ml) for 4 hr. Removal of the inorganic material by filtration and of the solvent under vacuum gave a viscous liquid which on addition of benzene gave a solid which was filtered. The filtrate was worked-up separately. The solid was recrystallized from benzene to give 0.05 g (3%) of bis-2,2'-benzothiazolyl (16) as colourless,glistening plates, melting at 300-301° (lit.[27] mp 300-301°).

The filtrate, after the removal of bis-2,2'-benzothiazolyl,was chromatographed over alumina. Elution with a mixture (4:1) of petroleum ether and benzene gave 0.25 g (18%) benzaldehyde isolated through its 2,4-dinitrophenylhydrazone derivative (0.68 g), mp 238°.(mixture mp). Further elution of the column,with a mixture (1:1) of petroleum ether and benzene,gave 0.9 g (55%) of benzothiazole (10) which was comparable with an authentic sample.

C In Refluxing Chloroform

A mixture of 2-hydrazinobenzothiazole (1 g, 6.0 mmol) and nickel peroxide (5 g) was refluxed in chloroform (200 ml) for 3 hr. Work-up of the mixture in the usual manner gave a viscous liquid which was chromatographed on alumina. Elution with a mixture (1:1) of benzene and petroleum ether gave a

solid which was recrystallized from benzene to give 0.1 g (11%) of 2,2'-azodibenzothiazole (17), mp 294° (lit.[28] mp 294°). Further elution of the column with the same solvent mixture gave 0.11 g (14%) of benzothiazole (10), bp 223-225° which was comparable with an authentic sample.

Oxidation of N-Aminophthalimide (24)

A mixture of N-aminophthalimide (1 g, 6.17 mmol) and nickel peroxide (5 g) was refluxed in benzene (200 ml) for 5 hr. Removal of the inorganic material and the solvent gave a solid, which was triturated with hot benzene. The benzene-insoluble portion was recrystallized from aqueous alcohol to give 0.4 g (44%) of phthalimide (28), mp 238° (mixture mp). Removal of the solvent from the benzene-soluble portion gave a product which was recrystallized from benzene to give 0.3 g (33%) of unchanged starting material, mp 204-205° (mixture mp).

Oxidation of N-(2-aminophenyl)-pyrrolidine (29)

A mixture of N-(2-aminophenyl)-pyrrolidine (1.5 g, 9.25 mmol) and nickel peroxide (6 g) was stirred in benzene for 6 hr at room temperature. Work-up of the mixture in the usual manner gave a red viscous liquid which was chromatographed over alumina. Elution with petroleum ether gave a solid which was recrystallized from petroleum ether to give

0.15 g (10%) of 2,2'-di-(N-pyrrolidino)-azobenzene (34), mp 177-178°.

Anal. Calcd for $C_{20}H_{24}N_4$: C, 75.00; H, 7.50; N, 17.50. Found: C, 74.77; H, 7.23; N, 17.50.

The uv spectrum (ethanol) of 34 shows the following absorption maxima: 226 nm (ϵ,23,100), 275 (17,850), 311 (5,950), 472 (10,700), 502 (13,000) and 530 (11,500).

The ir spectrum (KBr) of 34 did not show the presence of any N-H group.

Further elution of the column with a mixture (9:1) of benzene and ethyl acetate gave a solid which was recrystallized from cyclohexane to give 0.05 g (3%) of 1,2-trimethylenebenzimidazole (32) melting at 99-100° (mixture mp).[22]

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VITAE

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